

Nousari, Hossein C.; Deterding, Robin; Wójcicki, Henry; Aho, Sirpa; Uitto, Jouni; Hashimoto, Takashi; Anhalt, Grant J.  
 The New England Journal of Medicine  
 May 6, 1999; 340 (18), pp 1406-1410  
 LINE COUNT: 00386 WORD COUNT: 05339

## TEXT

...an overt or occult neoplasm and causes blisters. It is characterized by the presence of IgG autoantibodies that react against desmosomal and hemidesmosomal plakín proteins, (Ref. 2-5) desmosomal transmembrane proteins...

...stratified squamous epithelium results from acantholysis, the loss of cell-cell adhesion, induced by pathogenic antibodies against the desmogleins. (Ref. 6) The most commonly associated neoplasms are, in decreasing order of...

...effects induced by chemotherapy, neoplasia, and autoantibody-mediated pulmonary injury. (Ref. 7-16) Deposits of IgG in the bronchial epithelium which have sometimes been observed, (Ref. 17) suggest that autoantibody-mediated...

...on the genitals, trunk, and extremities. A skin-biopsy specimen showed acantholysis with deposition of IgG and complement on the surfaces of keratinocytes and along the basement-membrane zone. Serum autoantibodies characteristic of paraneoplastic pemphigus were detected at a titer of 10,000; their antigenic...

...that occurs in two variants: a benign, localized, hyaline vascular type and an aggressive multicentric plasma-cell type...

...cough, which was productive of white sputum. Skin and mucosal lesions remained in clinical remission. Serum autoantibodies characteristic of paraneoplastic pemphigus remained present at a titer of 250... showed changes resembling lichen planus and necrosis of the keratinocytes. Direct immunofluorescence showed deposition of IgG and complement on the keratinocyte surfaces and deposition of complement along the basement-membrane zone. Serum autoantibodies associated with paraneoplastic pemphigus were present at a titer of 1280; their antigenic specificity was confirmed by immunoprecipitation. The mucocutaneous lesions resolved slowly with the administration of 1.0 mg of prednisolone per kilogram per day...

...severe hypoxemia, and spirometry revealed severe airflow limitation (Table 1). Sputum cultures were negative for Mycobacterium tuberculosis and other bacteria. Bronchoscopy showed erythema and edema of the respiratory epithelial mucosa with...

...the mucocutaneous lesions appeared. When he died, paraneoplastic pemphigus autoantibodies were still present in the serum at a titer of 640. An autopsy was not performed...

...Brenn, periodic acid-Schiff, Giemsa, Fite, and pentachrome stains. Frozen sections were probed with fluoresceinated antibodies specific for IgG, IgA, IgM, complement, and fibrin. (Ref. 18)  
 Written informed consent was obtained from both patients for the...

...Serum samples from both patients were tested by indirect immunofluorescence with the use of monkey esophagus and murine bladder, heart, and liver as substrates. Serum from these patients, from a control patient with lymphoma-associated paraneoplastic pemphigus, and from a...

...as previously described. (Ref. 19) Additional radiolabeled extracts were prepared in an identical fashion from human respiratory epithelial cells (Cionetics, San Diego, Calif.) that were grown in bronchial epithelial-cell growth...

...bullous pemphigoid antigen 1, desmoplakin I and II, envoplakin, and periplakin were cloned from a human matchmaker complementary DNA library (Cionotech, Palo Alto, Calif.) by the polymerase chain reaction with the use of primers according to published techniques. (Ref. 5) Reactivity of serum to the fusion proteins was tested by immunoblotting...

...For passive transfer of IgG into mice, IgG was purified from specimens from Patient 1 (Ref. 1,20) and injected into neonatal mice...

...of choice for such passive-transfer studies because their small size allows reproduction of circulating IgG levels similar to those in the human disease and because their hairless skin facilitates the induction and observation of cutaneous blistering. After...

...sections were obtained. All epithelial surfaces were examined for signs of acantholysis and deposition of human IgG...row of tombstones (Fig. 1). A mixed inflammatory infiltrate consisting of lymphocytes, neutrophils, eosinophils, and plasma cells was present in the submucosa. Staining with specialized reagents did not reveal bacteria, fungi, mycobacteria, or *Pneumocystis carinii*. Pentachrome staining, which can reveal changes in elastic fiber and collagen indicative...

...no cytologic evidence of cytomegalovirus infection or cancer. Evaluation of frozen tissue showed deposition of IgG and complement in a linear manner on the respiratory-epithelial-cell surfaces and in a...

...of tombstones' characteristic of the loss of cell-cell attachment (acantholysis) mediated by the pemphigus antibody (hematoxylin and eosin, x400). \*\*FIGURE 2. Direct Immunofluorescence of the Endobronchial Biopsy Specimen from Patient 1. Linear deposition of IgG is visible on the surfaces of the respiratory epithelial cells (open arrow) as well as...

...deposition is identical to that seen in the epidermis of patients with paraneoplastic pemphigus (anti-human IgG, x400). \*\*FIGURE 2. Direct Immunofluorescence of the Endobronchial Biopsy Specimen from Patient 1. Linear deposition of IgG is visible on the surfaces of the respiratory epithelial cells (open arrow) as well as...

...Both patients' serum samples contained IgG autoantibodies that reacted to the epithelial surfaces and basement membrane of monkey esophagus as well as to murine urinary-bladder epithelial cells, intercalated disks of myocardium and hepatocyte desmosomes. Serum from both patients also contained antigens of 250, 230, 210 (a doublet), and 190 kd...

...was detected in the keratinocyte extracts but not in the respiratory epithelial extracts. The control serum from the patient with pemphigus vulgaris did not detect expression of the 130-kd pemphigus...

...Pemphigus Autoantibodies with Respiratory Epithelial Antigens. Immunoprecipitation was performed on metabolically labeled keratinocytes and normal human bronchial epithelial cells. Molecular-weight (MW) markers are shown at 200, 116, and 97 kd. Lanes 1 and 2 show control serum from a patient with paraneoplastic pemphigus. Serum from epidermal cells (lane 1) contains autoantibodies that recognize the paraneoplastic pemphigus antigen complex, with bands detected at 250, 230, 210, 190, and 170 kd. Serum from respiratory epithelial cells (lane 2) immunoprecipitates protein bands at 250, 230, 210 and 190...

... and 4 (Patient 1) and lanes 5 and 6 (Patient 2) show antigens recognized by serum from patients with paraneoplastic pemphigus and pulmonary involvement. Serum from both patients reacts with plakín antigens expressed by both keratinocytes (lanes 4 and 5...).

...7 shows results with respiratory epithelial cells from a patient with pemphigus vulgaris; this control serum fails to immunoprecipitate any of the antigens of the paraneoplastic pemphigus complex. This finding confirms...

...the pemphigus vulgaris antigen is not expressed by respiratory epithelial cells, as expected. This control serum also shows that the 170-kd antigen is expressed in epidermal cells, but not in...

...The serum samples reacted strongly to fusion proteins from the homologous tail region of envoplakin, reacted with...

...from neonatal mice showed cutaneous acantholytic blistering. We detected neither acantholysis nor specific deposition of human IgG in the bronchial epithelium despite the presence of human pemphigus autoantibodies in the serum at a titer of 1280...

...Pemphigus diseases of the skin are characterized by acantholytic blistering caused by the reaction of IgG autoantibodies against desmogleins. In pemphigus foliaceus, blisters are superficial; mucous membranes are never involved. Antibodies against desmoglein 1 are responsible for this limited form of the disease. In pemphigus vulgaris, patients also produce antibodies against desmoglein 3, and blisters form on both the skin and the mucous membranes. However...

...In patients with paraneoplastic pemphigus, pathogenic autoantibodies react against the desmogleins, but the antibodies are present at a low titer and can be detected only by a sensitive enzyme...

...proteins. (Ref. 4) The plakins are a group of sequence-related proteins that form the intracellular plaques of desmosomes and hemidesmosomes and that mediate attachment of the cytoskeletal intermediate filaments to...

...Bronchial epithelial tissue from these patients showed acantholysis and deposition of IgG autoantibodies on the cell surfaces. There is no evidence that antibodies against desmogleins play any part in the induction of respiratory lesions. In patients with pemphigus...

...We focused on antiplakin antibodies because desmogleins are evidently not involved in pulmonary injury and because our labeling studies showed...

...proved. Pulmonary epithelial lesions were not induced in mice either by infusion of pemphigus vulgaris IgG (with antibodies specific for desmoglein 3) (Ref. 20) or by IgG with antibodies against plakín proteins from patients with paraneoplastic pemphigus. However, there are potential explanations for these...

...First, plakín proteins are entirely intracellular. Although there is evidence that autoantibodies may enter living ... understood. Second, in passive-transfer studies in neonatal mice, the duration of exposure to the human autoantibodies is generally less than 48 hours. This is due to the behavior of the...

...be starved or eaten by the mother within 72 hours. Short-term exposure to transfused antibodies may not be sufficient to cause respiratory acantholysis. Third, in humans, pulmonary involvement in paraneoplastic...

...usually a late complication. It may be that additional inflammatory

events occur to allow these antibodies to bind within the desmosomal plaque of respiratory epithelium. The immaturity of neonatal bronchial epithelium...

...cytotoxic mechanisms may be important, and such mechanisms cannot be reproduced by passive transfer of IgG alone into the mice...

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...Puccetti A, Jarett L, Madai MP. Receptor-mediated cellular entry of nuclear localizing anti-DNA antibodies via myosin 1. *J Clin Invest* 1997;100:25-31.

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Set	Items	Description
S1	43	E1-E6
S2	22	RD (unique items)
S3	2	AU= LAHENZ J.
S4	21	E2-E6
S5	12	RD (unique items)
S6	0	S5 AND (IMMUNOG? OR IG? OR COLUST?)
S7	12	S5
S8	1	AU= BENITEZ, MAXIMO MARTINEZ
S9	2	E1-E2
S10	3	AU= HERNANDEZ, YAMILE LOPEZ
S11	4	AU= BOURZAC, JUAN FRANCISCO INFANTE
S12	2	RD (unique items)
S13	73946	MYCOBAC? AND (COLUST? OR IG? OR IMMUNOGLO? OR ANTI BO? OR - SERUM)
S14	9685	S13 AND (IGG OR IGA)
S15	2563	S14 AND (ADMIN? OR INTRA?)
S16	2563	S15 AND (MYCOBAC?)
S17	1301	S16 AND (LACTA? OR MAMMAL OR HUMAN)
S18	806	S17 AND (MONOCLONAL OR POLYCLONAL OR PLASMA OR SERUM OR CO- LUST?)
S19	797	S18 AND (HUMAN OR MAMMAL)
S20	57	S19 AND (((HUMAN) (W (COLOS? OR PLASMA OR SERUM OR IGA OR I- GG) OR ((MAMMAL) (W (COLOS? OR PLASMA OR SERUM OR IGA OR IGG- )))
S21	45	RD (unique items)
? s s21 and mycobac?	45	S21

631108 MYCOBAC?  
S22 45 S21 AND MYCOBAC?

## ABSTRACT:

Immune stimulating activity was compared for lipid vesicles consisting of the total polar lipids of an archaeon *Haloflex volcanii*, and the eubacteria *Planococcus* spp. and *Bacillus firmus*. Each total polar lipid extract readily formed liposomes of similar size, within which the protein antigen ovalbumin was entrapped, with comparable loading and...

...titers for all adjuvants, with memory recall responses that were significantly greater with the archaeal lipid (*H. volcanii* versus *Planococcus*). More striking, induction of cytotoxic T cell activity against the entrapped...

...secondary response after injections on days 0 and 21) in mice immunized with *Planococcus* spp. liposomes, but was sustained in mice immunized with *H. volcanii* archaeosomes. Surprisingly, antigen free-*Planococcus* liposomes evoked potent non-specific inflammatory cytokine production (IL-12 and IL-6) by dendritic cells...

...This suggested that overt inflammatory response might not necessarily aid sustenance of immunity. *B. firmus* liposomes consisted of phosphatidylglycerol, phosphatidylethanolamine and cardiolipin and was an ineffective CTL adjuvant, even for initiating a primary response. Considering that the polar lipids of *H. volcanii* and *Planococcus* spp. both consist of the same lipid classes (sulfolipids, phosphoglycerols, and cardiolipins), the unique ability of archaeosomes to maintain antigen-specific T cell immunity may be attributable to a property of the archaeal 2, 3- diphytanylglycerol lipid core.

DESCRIPTORS: Adjuvants; Liposomes; Immune response; Animal models; Immunization; Lymphocytes T; Cytokines; Interleukin 12; Interleukin 6; Lipids; Vaccination; Ovalbumin; *Haloflex volcanii*; *Planococcus*; *Bacillus firmus*

3/3, K/2 (Item 2 from file: 24)  
DIALOG File 24: CSA Life Sciences Abstracts  
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0002579884 IP ACCESSION NO: 5910066  
Archaeosomes as Self-Adjuvanting Delivery Systems for Cancer Vaccines

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Journal of Drug Targeting, v 11, n 8-10, p 515-524, 2003  
PUBLICATION DATE: 2003

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ISSN: 1061-186X  
FILE SEGMENT: Medical & Pharmaceutical Biotechnology Abstracts

Krishnan, L; Sprott, GD

ABSTRACT:

10563731a.txt

... cells is critical for protective vaccination against tumors, we compared the ability of various archaeosome lipid compositions to evoke a strong CD8 super(+) CTL response to entrapped antigen. Subcutaneous immunization of mice with ovalbumin (OVA) entrapped in all archaeosome lipid compositions evoked a primary (day 10) splenic CTL response indicating processing for MHC class I presentation. Interestingly, several polar lipid compositions from halophilic archaea were very potent to adjuvant this early CTL response. Despite this...

... protective CD8 super(+) response against B16OVA metastasis, indicating potential for targeting self, tumor antigens. Thus, lipid structural properties of archaea may differentially modulate primary, long-term and/or innate immunity, impacting...

3/3, K/3 (Item 3 from file: 24)  
DIALOG(R) File 24: CSA Life Sciences Abstracts  
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0002444549 IP ACCESSION NO: 5555773  
Safety of archaeosome adjuvants evaluated in a mouse model

Patel, GB; Omri, A; Deschatelets, L; Sprott, GD  
Department of Chemistry and Biochemistry, Laurentian University, 935 Ramsey  
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Journal of Liposome Research, v 12, n 4, p 353-372, November 2002  
PUBLICATION DATE: 2002

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0898-2104

FILE SEGMENT: Industrial & Applied Microbiology Abstracts (Microbiology A);  
Medical & Pharmaceutical Biotechnology Abstracts

Patel, GB; Omri, A; Deschatelets, L; Sprott, GD

#### ABSTRACT:

Archaeosomes, liposomes prepared from the polar ether lipids extracted from Archaea, demonstrate great potential as immunomodulating carriers of soluble antigens, promoting humoral and...

... immunity in the vaccinated host. The safety of unilamellar archaeosomes prepared from the total polar lipids (TPL) of Halobacterium salinarum, Methanobrevibacter smithii or Thermoplasma acidophilum was evaluated in female BALB/c...

... with any of the archaeosome adjuvants. None of the antigen-free archaeosomes elicited significant anti-lipid antibodies when subcutaneously injected (1 mg each at 0, 1, 2, and 4 weeks) in mice, although anti-H. salinarum lipid antibodies were detected. These anti-lipid antibodies cross-reacted with the TPL of T. acidophilum archaeosomes but not with the TPL of M. smithii archaeosomes nor with lipids of ester liposomes made from L- $\alpha$ -di-myristoyl phosphatidylcholine (DMPC), L- $\alpha$ -di-myristoyl phosphatidylglycerol (DMPG), and cholesterol (CHOL). In vitro

... 5 mg/mL concentration. At this concentration, H. salinarum archaeosomes and DMPC/DMPG/CHOL ester liposomes caused about 2% and 4% hemolysis, respectively. Based on this mouse model evaluation, archaeosomes are...

DESCRIPTORS: Vaccines; Safety; Liposomes; Hemolysis; Ovalbumin;  
archaeosomes; Halobacterium salinarum; Methanobrevibacter smithii;  
Thermoplasma acidophilum; Halobacterium salinarum

3/3, K/4 (Item 4 from file: 24)  
DIALOG File 24: CSA Life Sciences Abstracts  
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0002221849 I P ACCESSION NO: 5142120  
Molecular Mechanisms of Water and Solute Transport across Archaeobacterial  
Lipid Membranes

Mathai, JC; Sprott, GD; Zeidel, ML  
Renal-Electrolyte Division, Department of Medicine, University of  
Pittsburgh, Pittsburgh, Pennsylvania 15261, USA

Journal of Biological Chemistry, v 276, n 29, p 27266-27271, July 20, 2001  
PUBLICATION DATE: 2001

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ISSN: 0021-9258  
FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

Molecular Mechanisms of Water and Solute Transport across Archaeobacterial  
Lipid Membranes  
Mathai, JC; Sprott, GD; Zeidel, ML

# ABSTRACT:

... and both high and low extremes of temperature and pH. The bulk of  
their membrane lipids are polar, characterized by the archaeal  
structural features typified by ether linkage of the glycerol...

...Bacteria and Eukarya. Also unique to these bacteria are macrocyclic  
archaeol and membrane spanning caldarchaeol lipids that are found in  
some extreme thermophiles and methanogens. To define the barrier function  
of...

...on permeabilities, we investigated the water, solute (urea and  
glycerol), proton, and ammonia permeability of liposomes formed by  
these lipids. Both the macrocyclic archaeol and caldarchaeol  
lipids reduced the water, ammonia, urea, and glycerol permeability of  
liposomes significantly (6-120-fold) compared with  
diphytanylphosphatidylcholine liposomes. The presence of the ether  
bond and phytanyl chains did not significantly affect these permeabilities

...mobility of the midplane hydrocarbon region of the membranes formed by  
macrocyclic archaeol and caldarchaeol lipids play a significant role  
in reducing the permeability properties of the lipid membrane. In  
addition, it appears that substituting ether for ester bonds presents an  
additional barrier...

DESCRIPTORS: Membranes; Lipids; Liposomes; Permeability;  
cell membranes; glycerolipids; Archaea  
...SUBJ CATG: Lipids

DIALOG(R) File 24: CSA Life Sciences Abstracts  
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0002220333 IP ACCESSION NO: 5139043  
Immunization of mice with lipopeptide antigens encapsulated in novel liposomes prepared from the polar lipids of various Archaeobacteria elicits rapid and prolonged specific protective immunity against infection with the facultative intracellular pathogen, *Listeria monocytogenes*

Conlan, JW Krishnan, L; Willick, GE; Patel, GB; Sprott, GD  
Institute for Biological Sciences, National Research Council of Canada,  
Room 3065, 100 Sussex Drive, Ottawa, Ont., Canada K1A 0R6,  
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Vaccine, v 19, n 25-26, p 3509-3517, May 14, 2001  
PUBLICATION DATE: 2001

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ISSN: 0264-410X  
FILE SEGMENT: Bacteriology Abstracts (Microbiology B); Immunology Abstracts  
Immunization of mice with lipopeptide antigens encapsulated in novel liposomes prepared from the polar lipids of various Archaeobacteria elicits rapid and prolonged specific protective immunity against infection with the facultative...

Conlan, JW Krishnan, L; Willick, GE; Patel, GB; Sprott, GD

ABSTRACT:  
... represent a major advance for clinical vaccinology. The present study examines the ability of novel liposomes, termed archaeosomes, made from the polar lipids of various Archaeobacteria to act as self-adjuvanting vaccine delivery vehicles for such defined acellular...  
...prototypical intracellular pathogen. In this regard, all of the tested archaeosomes were superior to conventional liposomes.

DESCRIPTORS: Liposomes; Lymphocytes T; Vaccines; CD8 antigen; archaeosomes; Lipids; Immune response (cell-mediated); Adjuvants; *Listeria monocytogenes*; Archaeobacteria; *Listeria monocytogenes*  
...SUBJ CATG: Lipids; 06807

3/3,K/6 (Item 6 from file: 24)  
DIALOG(R) File 24: CSA Life Sciences Abstracts  
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0002184047 IP ACCESSION NO: 4851134  
The Potent Adjuvant Activity of Archaeosomes Correlates to the Recruitment and Activation of Macrophages and Dendritic Cells In Vivo

Krishnan, L; Sad, S; Patel, GB; Sprott, GD  
National Research Council, Institute for Biological Sciences, 100 Sussex Drive, Room 3016, Ottawa, Ontario, K1A 0R6, Canada,  
[mailto:lakshmi.krishnan@nrc.ca]

Journal of Immunology, v 166, n 3, p 1885-1893, February 1, 2001  
PUBLICATION DATE: 2001

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0022-1767

FILE SEGMENT: Immunology Abstracts; Bacteriology Abstracts (Microbiology B)

Krishnan, L; Sad, S; Patel, GB; Sprott, GD

## ABSTRACT:

... resulted in enhanced expression of MHC class II and B7.2 molecules. In contrast, conventional liposomes made from ester phospholipids failed to modulate the expression of these activation markers. APCs treated...

3/3, K/7 (Item 7 from file: 24)

DI ALCO (R) File 24: CSA Life Sciences Abstracts

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0002158898 IP ACCESSION NO: 4789414

Archaeosomes Induce Long-Term CD8 super(+) Cytotoxic T Cell Response to Entrapped Soluble Protein by the Exogenous Cytosolic Pathway, in the Absence of CD4 super(+) T Cell Help

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Journal of Immunology, v 165, n 9, p 5177-5185, November 1, 2000

PUBLICATION DATE: 2000

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0022-1767

FILE SEGMENT: Immunology Abstracts

Krishnan, L; Sad, S; Patel, GB; Sprott, GD

## ABSTRACT:

... 264). In contrast, administration of OVA with aluminum hydroxide or entrapped in conventional ester-phospholipid liposomes failed to evoke significant CTL response. The archaeosome-mediated CD8 super(+) T cell response was...

3/3, K/8 (Item 8 from file: 24)

DI ALCO (R) File 24: CSA Life Sciences Abstracts

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0002119776 IP ACCESSION NO: 4689447

Influence of Coenzyme Q10 on Tissue Distribution of Archaeosomes, and Pegylated Archaeosomes, Administered to Mice by Oral and Intravenous Routes

Omri, A; Makabi-Panzu, B; Agnew, BJ; Sprott, GD; Patel, GB

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Journal of Drug Targeting, v 7, n 5, p 383-392, 2000

PUBLICATION DATE: 2000

DOCUMENT TYPE: Journal Article  
 RECORD TYPE: Abstract  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ISSN: 1061-186X  
 FILE SEGMENT: Medical & Pharmaceutical Biotechnology Abstracts

Omri, A; Makabi-Panzu, B; Agnew, BJ; Sprott, GD; Patel, GB

ABSTRACT:

... The archaeosome formulations were prepared by a reverse-phase evaporation method using the total polar lipids from the archaeobacterium *Methanosarcina mazei*. In the case of oral gavage, the most striking observation...

...SUBJ CATG: Drug delivery vehicles (liposomes, cochleates, microspheres)

3/3,K/9 (Item 9 from file: 24)  
 DIALCO(R) File 24: CSA Life Sciences Abstracts  
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0002057229 IP ACCESSION NO: 4657064  
 Archaeobacterial Ether Lipid Liposomes (Archaeosomes) as Novel Vaccine and Drug Delivery Systems

Patel, GB; Sprott, GD  
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Critical Reviews in Biotechnology, v 19, n 4, p 317-357, 1999  
 PUBLICATION DATE: 1999

DOCUMENT TYPE: Journal Article; Review  
 RECORD TYPE: Abstract  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ISSN: 0738-8551  
 FILE SEGMENT: Medical & Pharmaceutical Biotechnology Abstracts

Archaeobacterial Ether Lipid Liposomes (Archaeosomes) as Novel Vaccine and Drug Delivery Systems

Patel, GB; Sprott, GD

ABSTRACT:

Liposomes are artificial, spherical, closed vesicles consisting of one or more lipid bilayer(s). Liposomes made from ester phospholipids have been studied extensively over the last 3 decades as artificial membrane models. Considerable interest has been generated for applications of liposomes in medicine, including their use as diagnostic reagents, as carrier vehicles in vaccine formulations, or...

...The objective of this article is to review the properties and potential applications of novel liposomes made from the membrane lipids of Archaeobacteria (Archaea). These lipids are unique and distinct from those encountered in Eukarya and Bacteria. Polar glycerolipids make up the bulk of the membrane lipids, with the remaining neutral lipids being primarily squalenes and other hydrocarbons. The polar

lipids consist of regularly branched, and usually fully saturated, phytanyl chains of 20, 25, or 40...

...carbons of the glycerol backbone(s). It has been shown only recently that total polar lipids of archaeobacteria, and purified lipid fractions therefrom, can form liposomes. We refer to liposomes made with any lipid composition that includes ether lipids characteristic of Archaeobacteria as archaeosomes to distinguish them from vesicles made from the conventional lipids obtained from eukaryotic or eubacterial sources or their synthetic analogs. In general, archaeosomes demonstrate relatively...

...archaeosomes by phagocytic cells can be up to 50-fold greater than that of conventional liposome formulations. Studies in mice have indicated that systemic administration of several test antigens entrapped within...

...archaeosome formulations indicate that they may offer a superior alternative to the use of conventional liposomes, at least for some biotechnology applications.

DESCRIPTORS: Lipids; Liposomes; Drug delivery; Vaccines; Archaeobacteria; Archaea; ether lipids  
...SUBJ CATG: Drug delivery vehicles (liposomes, cochleates, microspheres); 33000...

3/3, K/10 (Item 10 from file: 24)  
DIALOG(R) File 24: CSA Life Sciences Abstracts  
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0002053887 IP ACCESSION NO: 4652725  
Archaeosome vaccine adjuvants induce strong humoral, cell-mediated, and memory responses: Comparison to conventional liposomes and alum

Krishnan, L; Dicaire, CJ; Patel, GB; Sprott, GD  
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Infection and Immunity, v 68, n 1, p 54-63, January 2000  
PUBLICATION DATE: 2000

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ISSN: 0019-9567  
FILE SEGMENT: Bacteriology Abstracts (Microbiology B); Immunology Abstracts

Archaeosome vaccine adjuvants induce strong humoral, cell-mediated, and memory responses: Comparison to conventional liposomes and alum

Krishnan, L; Dicaire, CJ; Patel, GB; Sprott, GD

#### ABSTRACT:

Ether glycerolipids extracted from various archaeobacteria were formulated into liposomes (archaeosomes) possessing strong adjuvant properties. Mice of varying genetic backgrounds, immunized by different parenteral routes...

...those achieved with Freund's adjuvant and considerably more than those with alum or conventional liposomes

(phosphatidylcholine-phosphatidylglycerol-cholesterol, 1.8:0.2:1.5 molar ratio). Furthermore, antigen-specific immunoglobulin G1 (IgG1), IgG2a, and IgG2b isotype antibodies were all induced. Association of BSA with the lipid vesicles was required for induction of a strong response, and >80% of the protein was...

...Th1 and interleukin-4 (IL-4) (Th2) by spleen cells in vitro. In contrast, conventional liposomes induced little cell-mediated immunity, whereas alum stimulated only an IL-4 response. In contrast to alum and Freund's adjuvant, archaeosomes composed of Thermoplasma acidophilum lipids evoked a dramatic memory antibody response to the encapsulated protein (at approximately 300 days) after...

DESCRIPTORS: Adjuvants; Immune response (cell-mediated); Immune response (humoral); Liposomes; gamma-Interferon; Immunization; Bovine serum albumin; Alum; Archaeosome vaccine; Memory cells; Vaccines; Archaea

3/3, K/11 (Item 11 from file: 24)  
DIALOG(R) File 24: CSA Life Sciences Abstracts  
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0002001805 IP ACCESSION NO: 4567137  
Stability of liposomes prepared from the total polar lipids of Methanosarcina mazei is affected by the specific salt form of the lipids

Patel, GB; Agnew, BJ; Jarrell, HC; Spratt, GD  
Institute for Biological Sciences, National Research Council of Canada, 100  
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[mailto:girish.patel@nrc.ca]

Journal of Liposome Research, v 9, n 2, p 229-245, May 1999  
PUBLICATION DATE: 1999

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0898-2104

FILE SEGMENT: Medical & Pharmaceutical Biotechnology Abstracts;  
Bacteriology Abstracts (Microbiology B)

Stability of liposomes prepared from the total polar lipids of Methanosarcina mazei is affected by the specific salt form of the lipids

Patel, GB; Agnew, BJ; Jarrell, HC; Spratt, GD

#### ABSTRACT:

The total polar lipids (TPL) extracted from the archaeobacterium Methanosarcina mazei were predominantly in the form of sodium and...

...of the divalent cations, magnesium plus calcium decreased from about 11:1 to 2:1. Liposomes (archaeosomes) made from ns-TPL were unable to efficiently retain low molecular weight aqueous markers...

...to about 25% and 100% respectively. Except for some differences in phosphatidylserine and phosphatidylglycerol, the lipid compositions of ns-TPL, s-TPL, and the magnesium form of TPL were similar, as determined by thin layer chromatography of labeled lipids. Archaeosomes prepared from s-TPL and ns-TPL had super(31)P NMR spectra that were similar to each

other, but distinct from those of vesicles prepared from the ester lipid dimyristoylphosphatidylcholine. The types and relative proportions of cations associated with the lipids of *M. mazei* prior to their hydration and vesicle formation have a major influence, although other factors such as lipid composition may have an effect, on the permeability of the bilayer to low molecular weight...

DESCRIPTORS: Liposomes; Lipids; Methanosarcina mazei;  
Methanogenic archaea; Methanosarcina mazei  
... SUBJ CATG: Drug delivery vehicles (liposomes, cochleates,  
microspheres); 02731...

... Lipids

3/3, K/12 (Item 12 from file: 24)  
DIALOG(R) File 24: CSA Life Sciences Abstracts  
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0001891728 I.P. ACCESSION NO: 4403754  
Coenzyme Q10 in vesicles composed of archaeal ether lipids or  
conventional lipids enhances the immuno-adjuvantivity to encapsulated  
protein

Makabi-Panzu, B; Sprott, GD\*; Patel, GB  
National Research Council, Institute for Biological Sciences, 100 Sussex  
Drive, Ottawa, Ontario, Canada K1A 0R6

Vaccine, v 16, n 16, p 1504-1510, October 1998  
PUBLICATION DATE: 1998

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ISSN: 0264-410X  
FILE SEGMENT: Immunology Abstracts; Medical & Pharmaceutical Biotechnology  
Abstracts

Coenzyme Q10 in vesicles composed of archaeal ether lipids or  
conventional lipids enhances the immuno-adjuvantivity to encapsulated  
protein

Makabi-Panzu, B; Sprott, GD\*; Patel, GB

#### ABSTRACT:

Cellular accumulation, tissue distribution, and immuno-adjuvantivity were evaluated for liposomal CoQ10 prepared from either distearoylphosphatidylcholine:dicetylphosphate:cholesterol (4:1:5, mol. ratio) (conventional liposomes) or from the total polar lipids of the archaeon *Methanosarcina mazei* (archaeosomes). Liposomal CoQ10 vesicles of approximately 100 nm diameter, containing up to 179 nmol of CoQ10 per mg of lipid have been evaluated using J774A.1 macrophages and Balb/c mice. Archaeosomes uptake by J774A.1 macrophages was better than with the conventional liposome, and the incorporation of CoQ10 enhanced the uptake of both lipid vesicle types. All vesicle types were detected in the liver and spleen of mice (4-27% of injected dose) within 3 h of intraperitoneal injection. Moreover, incorporation of CoQ10 into lipid vesicles enhanced the immuno-adjuvantivity of both conventional liposomes and archaeosomes, to achieve approximately a doubling in the titres of BSA-specific antibody in... hydrophobicity and opsonization changes induced by the presence of CoQ10

10563731a.txt

in vesicles. We suggest that liposomal CoQ10 has potential as a new generation of vaccine delivery system to enhance the immune...

DESCRIPTORS: Adjuvants; Liposomes; Membrane vesicles; Vaccines; Macrophages; coenzyme Q10; Methanosarcina mazei

3/3, K/13 (Item 13 from file: 24)  
DI ALCOR File 24: CSA Life Sciences Abstracts  
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0001791080 IP ACCESSION NO: 4209389  
Archaeosomes as novel antigen delivery systems

Sprott, GD; Tolson, DL; Patel, GB  
Institute for Biological Sciences, National Research Council of Canada, 100  
Sussex Drive, Ottawa, Ont. K1A 0R6, Canada

FEMS Microbiology Letters, v 154, n 1, p 17-22, September 1997  
PUBLICATION DATE: 1997

PUBLISHER: ELSEVIER SCIENCE B. V.

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Citation  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ISSN: 0378-1097  
FILE SEGMENT: Bacteriology Abstracts (Microbiology B); Immunology Abstracts

Sprott, GD; Tolson, DL; Patel, GB

DESCRIPTORS: Vaccines; cholera toxin B; liposomes; archaeal ether lipids; immune response (humoral); albumin; lipids; Adjuvants; Methanobrevibacter smithii; archaeosomes; Vibrio cholerae; Methanobrevibacter smithii

3/3, K/14 (Item 14 from file: 24)  
DI ALCOR File 24: CSA Life Sciences Abstracts  
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0001787833 IP ACCESSION NO: 4224625  
Uptake of archaeobacterial liposomes and conventional liposomes by phagocytic cells

Tolson, DL; Latta, RK; Patel, GB; Sprott, GD  
Inst. for Biol. Sci., Natl. Res. Council Canada, 100 Sussex Dr., Ottawa, ON  
K1A 0R6, Canada

Journal of Liposome Research, v 6, n 4, p 755-776, November 1996  
PUBLICATION DATE: 1996

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ISSN: 0898-2104  
FILE SEGMENT: Bacteriology Abstracts (Microbiology B); Industrial & Applied Microbiology Abstracts (Microbiology A); Medical & Pharmaceutical Biotechnology Abstracts

Uptake of archaeobacterial liposomes and conventional liposomes

by phagocytic cells

Tolson, DL; Latta, RK; Patel, GB; Sprott, GD

ABSTRACT:

Liposomes in the 200 nm size range were prepared from the ether lipids extracted from various Archaeobacteria (coined archaeosomes), and from conventional lipids. The entrapment of peroxidase or carboxyfluorescein was used to compare the in vitro uptake of various liposomes by murine peritoneal macrophages, J774A.1 macrophages and several non phagocytic cell lines. While liposomes composed of ester lipids di palmitoyl phosphatidylcholine, or di myristoyl phosphatidylcholine: di myristoyl phosphatidyl glycerol: cholesterol (1.8:0.2:1.5, molar ratio) were taken...

...cells, using high doses of three representative types of archaeosomes and one type of conventional-liposome. Therefore, archaeosomes may be well suited to applications where phagocytic cells are a target site.

DESCRIPTORS: Liposomes; Phagocytosis; Macrophages; Archaeobacteria; archaeobacteria

...SUBJ CATG: Drug delivery vehicles (liposomes, cochleates, microspheres)

3/3, K/15 (Item 15 from file: 24)  
DIALOG(R) File 24: CSA Life Sciences Abstracts  
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0001751006 IP ACCESSION NO: 4095257  
Structural features of ether lipids in the archaeobacterial thermophiles *Pyrococcus furiosus*, *Methanopyrus kandleri*, *Methanothermobacter* *fervidus*, and *Sulfolobus acidocaldarius*

Sprott, GD; Agnew, BJ; Patel, GB  
Inst. for Biol. Sci., Natl. Res. Council, Canada, 100 Sussex Dr., Ottawa, ON  
K1A 0R6, Canada

Canadian Journal of Microbiology/Revue Canadienne de Microbiologie, v 33,  
n 5, p 467-476, May 1997  
PUBLICATION DATE: 1997

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English; French  
ISSN: 0008-4166  
ASFA NO: CS9717783

FILE SEGMENT: Bacteriology Abstracts (Microbiology B)  
Structural features of ether lipids in the archaeobacterial thermophiles *Pyrococcus furiosus*, *Methanopyrus kandleri*, *Methanothermobacter* *fervidus*, and *Sulfolobus acidocaldarius*

Sprott, GD; Agnew, BJ; Patel, GB

ABSTRACT:

The ether lipids of several thermophilic archaea (archaeobacteria) were compared by negative-ion fast atom bombardment mass spectrometry. The major polar lipids in extracts of *Pyrococcus furiosus* were assigned as archaeol lipids (phosphatidylglycerol diether, *m/z* 805; phosphatidylinositol diether, *m/z* 893; and diglycosyl diether, *m/z* 975) and

10563731a.txt

cal dar chaeol lipi ds (di glycosyl phosphati dyl glycerol tetra ether, m/z 1778; and di glycosyl phosphati dyl inositol tetra ether, m/z 1866). The polar lipi ds of Methanopyrus kandleri were primarily glycolipids consisting of a series of archaeol lipi ds with one to six hexose units, composed primarily of mannose (mannose: glucose 9:1); phospholipids consisting of archaeol lipi ds (phosphatidyl inositol di ether; and a novel phosphatidyl choline di ether, m/z 802.7), and phosphoglycolipids as minor cal dar chaeol lipi ds (primarily di glycosyl phosphati dyl glycerol tetra ether). Methanothermus fervidus extracts contained archaeol lipi ds (phosphatidyl inositol di ether; di glycosyl di ether; and acetyl di glycosyl di ether, m/z 1016), and cal dar chaeol lipi ds (glycosyl phosphati dyl inositol tetra ether, m/z 1704; di glycosyl phosphati dyl inositol tetra ether; and acetyl di glycosyl phosphati dyl inositol tetra ether, m/z...

...residue occurred commonly in this thermophile and increased as cells entered the stationary growth phase. Lipid extracts of Sulfolobus acidocaldarius contained detectable amounts of archaeol and hydroxyarchaeol analogs of phosphatidyl inositol, phosphatidyl glycerol, and phosphatidyl ethanolamine lipi ds, in addition to the dominant cal dar chaeol lipi ds already reported. All four thermophiles contained both archaeol and cal dar chaeol lipi ds and phosphoinositol head groups, but no single structural entity uniquely separated their lipi ds from those found previously in mesophilic archaea. By contrast, extremely halophilic archaea appear to be distinguished from the thermophilic archaea by the presence of a major phosphatidyl glyceronethyl phosphate lipi d.

DESCR PTORS: thermophilic bacteria; halophilic bacteria; Chemical analysis; Biochemistry; lipi ds; bacteria; hydrothermal springs; Pyrococcus furiosus; Methanopyrus kandleri; Methanothermus fervidus; Sulfolobus acidocaldarius  
IDENTIFIERS: ether lipi ds; hydrothermal springs; Sulfolobus acidocaldarius; thermophilic bacteria; halophilic bacteria  
...SUBJ CATG: Lipi ds

3/3, K/16 (Item 16 from file: 24)  
DIALOG File 24: CSA Life Sciences Abstracts  
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0001674255 IP ACCESSION NO: 3990014  
Heat sterilization of archaeal liposomes

Choquet, CG; Patel, GB; Sprott, GD\*  
Institute for Biological Sciences, National Research Council of Canada,  
Ottawa, ON K1A 0R6, Canada

Canadian Journal of Microbiology/Revue Canadienne de Microbiologie, v 42  
n 2, p 183-186, February 1996  
PUBLICATION DATE: 1996

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English; French  
ISSN: 0008-4166  
FILE SEGMENT: Agricultural & Environmental Biotechnology Abstracts

Heat sterilization of archaeal liposomes

Choquet, CG; Patel, GB; Sprott, GD\*

## ABSTRACT:

Thermal stabilities were compared between liposomes prepared from the ether lipids extracted from various archaeobacteria and liposomes composed of ester lipids. Leakage of entrapped carboxyfluorescein from the liposomes exposed to 121 degree C indicated a marked stability of certain ether liposomes, comparable or superior to cholesterol-stabilized liposomes prepared from the saturated synthetic lipids dimyristoyl phosphatidylcholine and dimyristoyl phosphatidylglycerol. The heat stability of diether liposomes could be increased by the inclusion of tetraether lipids.

DESCRIPTORS: liposomes; heat treatments; drug delivery; archaeobacteria

IDENTIFIERS: ester lipids; cholesterol

3/3, K/17 (Item 17 from file: 24)  
 DIALOG(R) File 24: CSA Life Sciences Abstracts  
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0001504595 IP ACCESSION NO: 3760445  
 Stability of pressure-extruded liposomes made from archaeobacterial ether lipids

Choquet, CG; Patel, GB; Beveridge, TJ; Sprott, GD\*  
 Inst. Biol. Sci., Natl. Res. Council, Canada (NRCC), Ottawa, ON K1A 0R6,  
 Canada

Applied Microbiology and Biotechnology, v 42, n 2-3, p 375-384, 1994  
 ADDL SOURCE INFO: Applied Microbiology and Biotechnology [APPL. MICROBIOL. BIOTECHNOL.], vol. 42, no. 2-3, pp. 375-384, 1994  
 PUBLICATION DATE: 1994

DOCUMENT TYPE: Journal Article  
 RECORD TYPE: Abstract  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ISSN: 0175-7598  
 FILE SEGMENT: Agricultural & Environmental Biotechnology Abstracts

Stability of pressure-extruded liposomes made from archaeobacterial ether lipids

Choquet, CG; Patel, GB; Beveridge, TJ; Sprott, GD\*

## ABSTRACT:

Ether lipids were obtained from a wide range of archaeobacteria grown at extremes of pH, temperature, and salt concentration. With the exception of *Sulfolobus acidocaldarius*, unilamellar and/or multilamellar liposomes could be prepared from emulsions of total polar lipid extracts by pressure extrusion through filters of various pore sizes. Dynamic light scattering, and electron microscopy revealed homogeneous liposome populations with sizes varying from 40 to 230 nm depending on both the lipid source and the pore size of the filters. Leakage rates of entrapped fluorescent or radioactive compounds established that those archaeobacterial liposomes that contained tetraether lipids were the most stable to high temperatures, alkaline pH, and serum proteins. Most ether liposomes were stable to phospholipase A sub(2), phospholipase B and pancreatic lipase. These properties of archaeobacterial liposomes make them attractive for applications in

biotechnology.

DESCRIPTORS: archaeobacteria; liposomes; lipids; Sulfolobus  
acidocaldarius  
... SUBJ CATG: Lipids and sterols

3/3, K/18 (Item 18 from file: 24)  
DIALOG(R) File 24: CSA Life Sciences Abstracts  
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0001491071 I.P. ACCESSION NO: 3741723  
The ether lipids of *Methanosarcina mazei* and other *Methanosarcina*  
species, compared by fast atom bombardment mass spectrometry

Sprott, GD; Dicaire, CJ; Patel, GB  
Inst. Biol. Sci., Natl. Res. Council, Canada, Ottawa, ON K1A 0R6, Canada

Canadian Journal of Microbiology/Revue Canadienne de Microbiologie, v 40,  
n 10, p 837-843, 1994

ADDITIONAL SOURCE INFO: Canadian Journal of Microbiology/Revue Canadienne de  
Microbiologie [CAN. J. MICROBIOL./REV. CAN. MICROBIOL.], vol. 40, no. 10,  
pp. 837-843, 1994

PUBLICATION DATE: 1994

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English; French

ISSN: 0008-4166

FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

The ether lipids of *Methanosarcina mazei* and other *Methanosarcina*  
species, compared by fast atom bombardment mass spectrometry

Sprott, GD; Dicaire, CJ; Patel, GB

#### ABSTRACT:

The total lipids of *Methanosarcina mazei* accounted for 4.0% of the  
cell dry mass, and 90% of these were polar lipids. Nearly all of the  
polar fraction consisted of diether (2,3-di-O-phytanyl-sn...

...hydroxydiether analogs of phosphatidylglycerol, phosphatidylinositol,  
phosphatidylserine, and phosphatidylethanolamine. Several highly  
fluorescent trace components in the lipid extracts were purified and  
partially characterized by mass spectrometry. Fast atom bombardment mass  
spectrometry of total lipid extracts provided data to establish a  
close relationship among the polar lipids present in *Methanosarcina*  
*mazei*, *Methanosarcina thermophila*, *Methanosarcina acetivorans*,  
*Methanosarcina barkeri* Fusaro, and *Methanosarcina barkeri* MS.

DESCRIPTORS: lipids; mass spectroscopy; *Methanosarcina mazei*;  
*Methanosarcina barkeri*; *Methanosarcina thermophila*; *Methanosarcina*  
*acetivorans*  
... SUBJ CATG: Lipids

3/3, K/19 (Item 19 from file: 24)  
DIALOG(R) File 24: CSA Life Sciences Abstracts  
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0001268225 I.P. ACCESSION NO: 2984633  
Hydroxydiether lipid structures in *Methanosarcina* spp. and  
*Methanococcus voltae*.

Sprott, GD; Di caire, CJ; Choquet, CG; Patel, GB; Ekiel, I  
Inst. Biol. Sci., 100 Sussex Dr., Ottawa, ON K1A 0R6, Canada

Applied and Environmental Microbiology, v 59, n 3, p 912-914, 1993  
ADDL. SOURCE INFO: Applied and Environmental Microbiology [APPL. ENVIRON.  
MICROBIOL.], vol. 59, no. 3, pp. 912-914, 1993  
PUBLICATION DATE: 1993

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ISSN: 0099-2240  
FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

Hydroxydiether lipid structures in Methanosarcina spp. and  
Methanococcus voltae .

Sprott, GD; Di caire, CJ; Choquet, CG; Patel, GB; Ekiel, I

ABSTRACT:

Hydroxylated diether lipids are the most abundant lipids in  
Methanosarcina acetivorans, Methanosarcina thermophila, and Methanosarcina  
barkeri MS and Fusaro, regardless of the substrate used for growth.  
Structural analysis of the lipid moiety freed of polar head groups  
revealed that the hydroxydiether lipids of all the Methanosarcina  
strains were hydroxylated at position 3 of sn-2 phytanyl chains...

DESCRIPTORS: lipids; Methanosarcina; Methanococcus voltae  
IDENTIFIERS: hydroxydiether lipids  
... SUBJ CATG: Lipids

3/3, K/20 (Item 20 from file: 24)  
DIALCOG File 24: CSA Life Sciences Abstracts  
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0001263243 I.P. ACCESSION NO: 2978066  
Metabolic pathways in Methanococcus jannaschii and other methanogenic  
bacteria.

Sprott, GD; Ekiel, I; Patel, GB  
Inst. Biol. Sci., Natl. Res. Council, Canada, 100 Sussex Drive, Ottawa, ON  
K1A 0R6, Canada

Applied and Environmental Microbiology, v 59, n 4, p 1092-1098, 1993  
ADDL. SOURCE INFO: Applied and Environmental Microbiology [APPL. ENVIRON.  
MICROBIOL.], vol. 59, no. 4, pp. 1092-1098, 1993  
PUBLICATION DATE: 1993

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ISSN: 0099-2240  
FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

Sprott, GD; Ekiel, I; Patel, GB

ABSTRACT:

... revalonate were incorporated when supplied to the growth medium  
 Lysine was preferentially incorporated into the lipid fraction,  
 suggesting a role as a phytanyl chain precursor.  
 ? e au=krishnan, l ?

Ref	Items	Index-term
E1	16	AU=KRI SHNAN, L. K.
E2	113	AU=KRI SHNAN, L. V.
E3	0	* AU=KRI SHNAN, L?
E4	70	AU=KRI SHNAN, LAKSHM
E5	1	AU=KRI SHNAN, LAKSHM V.
E6	2	AU=KRI SHNAN, LAKSHMY
E7	1	AU=KRI SHNAN, LAKSHMY A.
E8	1	AU=KRI SHNAN, LALI THA
E9	225	AU=KRI SHNAN, LALI THA
E10	1	AU=KRI SHNAN, LATA
E11	2	AU=KRI SHNAN, LATA A
E12	2	AU=KRI SHNAN, LATA A.

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16	AU=KRI SHNAN, L. K.
113	AU=KRI SHNAN, L. V.
0	AU=KRI SHNAN, L?
70	AU=KRI SHNAN, LAKSHM
1	AU=KRI SHNAN, LAKSHM V.
2	AU=KRI SHNAN, LAKSHMY
202	E1-E6

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6/3, K/1 (Item 1 from file: 24)

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0003382979 I P ACCESSI ON NO: 8554484

Archaeosome adjuvants: Immunological capabilities and mechanism(s) of action

Krishnan, Lakshmi; Sprott, Dennis

National Research Council-Institute for Biological Sciences, Ottawa, ON, Canada K1A 0R6, [mailto:Lakshmi.Krishnan@nrc-cnrc.gc.ca]

Vaccine, v 26, n 17, p 2043-2055, April 2008

PUBLICATION DATE: 2008

PUBLISHER: Elsevier Science, The Boulevard Langford Lane Kidlington Oxford OX5 1GB UK, [mailto:usinfo-f@elsevier.com], [URL:http://www.elsevier.nl]

DOCUMENT TYPE: Journal Article  
 RECORD TYPE: Abstract  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ISSN: 0264-410X  
 ELECTRONIC ISSN: 1873-2518  
 FILE SEGMENT: Bacteriology Abstracts (Microbiology B); Immunology Abstracts  
 Krishnan, Lakshmi; Sprott, G Dennis

## ABSTRACT:

Archaeosomes (liposomes comprised of glycerolipids of Archaea) constitute potent adjuvants for the induction of Th1, Th2 and CD8 super(+) T cell responses to the entrapped soluble antigen. Archaeal lipids are uniquely constituted of ether-linked isoprenoid phytanyl cores conferring stability to the membranes. Additionally, varied head groups displayed on the glycerol-lipid cores facilitate unique immunostimulating interactions with mammalian antigen-presenting cells (APCs). The polar lipid from the archaeon, *Methanobrevibacter smithii* has been well characterized for its adjuvant potential, and is...

... DESCRIPTORS: Antigen presentation; Antigen-presenting cells; CD8 antigen; Cancer; Cytokines; Helper cells; Immunological memory; Infection; Inflammation; Lipids; Liposomes; Lymphocytes T; Major histocompatibility complex; Memory cells; Phospholipids; Serine; Terpenes; Therapeutic applications; Vaccines; phosphatidylserine; Archaea...

6/3, K/2 (Item 2 from file: 24)  
 DIAGNOSTIC File 24: CSA Life Sciences Abstracts  
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0003014138 I.P. ACCESSION NO: 7289082  
 Rapid Clonal Expansion and Prolonged Maintenance of Memory CD8 super(+) T Cells of the Effector (CD44 super(high) CD62L super(low)) and Central (CD44 super(high) CD62L super(high)) Phenotype by an Archaeosome Adjuvant Independent of TLR2

Krishnan, Lakshmi; Gurnani, Komal; Dicaire, Chantal J; van Faassen, Henk; Zafer, Ahmed; Kirschning, Carsten J; Sad, Subash; Sprott, G Dennis  
 National Research Council-Institute for Biological Sciences, Ottawa, Ontario, Canada. Department of Biochemistry, Microbiology, and Immunology, University of Ottawa, Ottawa, Ontario, Canada. Institute for Microbiology, Immunology, and Hygiene, Technical University, Munich, Germany

Journal of Immunology, v 178, n 4, p 2396-2406, February 2007  
 PUBLICATION DATE: 2007

PUBLISHER: American Association of Immunologists, 9650 Rockville Pike  
 Bethesda MD 20814-3998 USA, [URL: <http://www.jimmunol.org/>]

DOCUMENT TYPE: Journal Article  
 RECORD TYPE: Abstract  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ISSN: 0022-1767  
 FILE SEGMENT: Bacteriology Abstracts (Microbiology B); Immunology Abstracts

Krishnan, Lakshmi; Gurnani, Komal; Dicaire, Chantal J; van Faassen, Henk; Zafer, Ahmed; Kirschning, Carsten J; Sad...

ABSTRACT:

... super(+) T cells were induced in TLR2-deficient mice, suggesting nonengagement of TLR2 by archaeal lipids. Thus, an archaeosome adjuvant vaccine represents an alternative to live vectors for inducing CD8 super...

DESCRIPTORS: Adjuvants; Antigen presentation; Blood; CD8 antigen; Effector cells; Histocompatibility antigen H-2; Immunization; Immunological memory; Lipids; Lymphocytes T; Memory cells; Spleen; TLR2 protein; Toll-like receptors; Vaccines; Vesicles; double prime T...

6/3, K/3 (Item 3 from file: 24)  
DIALOG(R) File 24: CSA Life Sciences Abstracts  
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0002606667 IP ACCESSION NO: 5992116  
Activation of Dendritic Cells by Liposomes Prepared from  
Phosphatidylinositol Mannosides from *Mycobacterium bovis* Bacillus Calmette-  
Guerin and Adjuvant Activity In Vivo

Sprott, GDennis; Di caire, Chantal J; Gurnani, Komal; Sad, Subash;  
Krishnan, Lakshmi  
Institute for Biological Sciences, National Research Council, Ottawa,  
Ontario, Canada

Infection and Immunity, v 72, n 9, p 5235-5246, September 2004  
PUBLICATION DATE: 2004

PUBLISHER: American Society for Microbiology, 1752 N Street N.W  
Washington, DC 20036 USA, [URL: <http://www.asm.org/>]

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ISSN: 0019-9567  
FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

Activation of Dendritic Cells by Liposomes Prepared from  
Phosphatidylinositol Mannosides from *Mycobacterium bovis* Bacillus Calmette-  
Guerin and Adjuvant Activity In Vivo

Sprott, GDennis; Di caire, Chantal J; Gurnani, Komal; Sad, Subash;  
Krishnan, Lakshmi

ABSTRACT:

Liposome vesicles could be formed at 65 degree C from the chloroform-soluble, total polar lipids (TPL) extracted from *Mycobacterium bovis* bacillus Calmette-Guerin (BCG). Mice immunized with ovalbumin (OVA) entrapped in TPL liposomes produced both anti-OVA antibody and cytotoxic T lymphocyte responses. Murine bone marrow-derived dendritic...

... 6 (IL-6), IL-12, and tumor necrosis factor upon exposure to antigen-free TPL liposomes. Three phosphoglycerolipids and three phospholipids comprising 96% of TPL were identified as phosphatidylinositol di mannoside, palmitoyl-phosphatidylinositol di mannoside, phosphatidylinositol di palmitoyl-phosphatidylinositol di mannoside, phosphatidylinositol,

phosphatidylethanolamine, and cardiolipin. The activation of dendritic cells by liposomes prepared from each purified lipid component of TPL was evaluated in vitro. A basal activity of phosphatidylinositol liposomes to activate proinflammatory cytokine production appeared to be attributable to the tuberculosteric fatty acyl 19:0 chain characteristic of mycobacterial glycerolipids, as similar lipids lacking tuberculosteric chains showed little activity. Phosphatidylinositol di-mannoside was identified as the primary lipid that activated dendritic cells to produce amounts of proinflammatory cytokines several times higher than the...

...induction levels of IL-6 and IL-12. Further, OVA entrapped in palmitoyl-phosphatidylinositol di-mannoside liposomes was delivered to dendritic cells for major histocompatibility complex class I presentation more effectively than TPL OVA-liposomes. BCG liposomes containing mannose lipids caused up-regulation of costimulatory molecules and CD40. Thus, the inclusion of pure phosphatidylinositol mannoses of BCG in lipid vesicle vaccines represents a simple and efficient option for targeting antigen delivery and providing immune...

DESCRIPTORS: Dendritic cells; Liposomes; Immunization; BCG; phosphoglycerolipids; phosphatidylinositol; phosphatidylethanolamine; cardiolipin; Immune response; Interleukin 6; Interleukin 12; Tumor necrosis factor...

6/3, K/4 (Item 4 from file: 24)  
DIALOG(R) File 24: CSA Life Sciences Abstracts  
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0002592371 IP ACCESSION NO: 5946009  
Phosphatidylserine Receptor-Mediated Recognition of Archaeosome Adjuvant Promotes Endocytosis and MHC Class I Cross-Presentation of the Entrapped Antigen by Phagosome-to-Cytosol Transport and Classical Processing

Gurnani, Korral; Kennedy, Jessica; Sad, Subash; Sprott, Dennis;  
Krishnan, Lakshmi  
National Research Council of Canada, Institute for Biological Sciences,  
Ottawa, Ontario, Canada

Journal of Immunology, v 173, n 1, p 566-578, July 1, 2004  
PUBLICATION DATE: 2004

PUBLISHER: American Association of Immunologists, 9650 Rockville Pike  
Bethesda MD 20814-3998 USA, [URL: <http://www.jimmunol.org/>]

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ISSN: 0022-1767  
FILE SEGMENT: Immunology Abstracts

Gurnani, Korral; Kennedy, Jessica; Sad, Subash; Sprott, Dennis;  
Krishnan, Lakshmi

ABSTRACT:  
... Ag. We analyzed the processing pathway of OVA entrapped in archaeosomes composed of *Methanobrevibacter smithii* lipids, high in archaeidylserine (OVA-archaeosomes). In vitro, OVA-archaeosomes stimulated spleen cells from OVA-TCR...

10563731a.txt

...or FcRs lacked effect, indicating specific recognition of the  
archaeitidylserine head group of M. smithii lipids by APCs. In  
addition, inhibitors of endosomal acidification blocked MHC class I  
processing of OVA...

6/3, K/5 (Item 1 from file: 399)

DI ALCOG R) File 399: CA SEARCH(R)

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148305999 CA: 148(14)305999x CONFERENCE PROCEEDING

Archaeosome vaccine adjuvants for cross-priming CD8+ T-cell immunity

AUTHOR(S): Krishnan, Lakshmi; Sprott, G. Dennis

LOCATION: Institute for Biological Sciences, National Research Council of  
Canada, Ottawa, ON, Can.,

JOURNAL: Vaccine Adjuvants Delivery Syst. (Vaccine Adjuvants and Delivery  
Systems) EDITOR: Singh, Manmohan (Ed), DATE: 2007 PAGES: 263-294

CODEN: 69KEOD LANGUAGE: English PUBLISHER: John Wiley & Sons, Inc.,  
Hoboken, N. J

6/3, K/6 (Item 2 from file: 399)

DI ALCOG R) File 399: CA SEARCH(R)

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147449032 CA: 147(21)449032d PATENT

Synthetic archaeal glyceroglycolipid adjuvants

INVENTOR(AUTHOR): Sprott, Dennis; Whitfield, Dennis; Krishnan, Lakshmi

LOCATION: Can.,

ASSIGNEE: National Research Council of Canada

PATENT: PCT International ; WO 2007112567 A1 DATE: 20071011

APPLICATION: WO 2007CA530 (20070330) \*US 2006PV787170 (20060330) \*US  
2006PV791225 (20060412)

PAGES: 98pp. CODEN: PIXD2D LANGUAGE: English

PATENT CLASSIFICATIONS:

IPC/8 + Level Value Position Status Version Action Source Office:

A61K 0015/04 A I F B 20060101 H CA

A61K 0039/39 A I L B 20060101 H CA

A61K 0047/24 A I L B 20060101 H CA

A61K 0047/26 A I L B 20060101 H CA

A61K 0047/28 A I L B 20060101 H CA

A61K 0009/127 A I L B 20060101 H CA

A61P 0031/00 A I L B 20060101 H CA

A61P 0035/00 A I L B 20060101 H CA

A61P 0037/04 A I L B 20060101 H CA

DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BH; BR; BW;  
BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; EG; ES; FI; GB;  
GD; GE; GH; GM; GT; HN; HR; HU; ID; IL; IN; IS; JP; KE; KG; KM; KN; KP; KR;  
KZ; LA; LC; LK; LR; LS; LT; LU; LY; MA; MD; MG; MK; MN; MW; MX; MY; MZ; NA;  
NG; NI; NO; NZ; OM; PG; PH; PL; PT; RO; RS; RU; SC; SD; SE; SG; SK; SL; SM;  
SV; SY; TJ; TM; TN; TR; TT; TZ; UA; UG DESIGNATED REGIONAL: AT; BE; BG; CH;  
CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; HU; IE; IS; IT; LT; LU; LV; MC;  
MT; NL; PL; PT; RO; SE; SI; SK; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW;  
ML; MR; NE; SN; TD; TG; BW; GH; GM; KE; LS; MW; MZ; NA; SD; SL; SZ; TZ; UG;  
ZM; ZW AM; AZ; BY; KG; KZ; MD; RU; TJ; TM

6/3, K/7 (Item 3 from file: 399)

DI ALCOG R) File 399: CA SEARCH(R)

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146204273 CA: 146(11)204273 JOURNAL

Rapid Clonal Expansion and Prolonged Maintenance of Memory CD8+ T Cells

Page 24

10563731a.txt  
of the Effector (CD44highCD62Low) and Central (CD44highCD62Lhigh)  
Phenotype by an Archaeosome Adjuvant Independent of TLR2  
AUTHOR(S): Krishnan, Lakshmi; Gurnani, Komal; Dicaire, Chantal J.; van  
Faassen, Henk; Zafer, Ahmed; Kirschning, Carsten J.; Sad, Subash; Sprott,  
G. Dennis  
LOCATION: Institute for Biological Sciences, National Research Council,  
Ottawa, ON, Can.,  
JOURNAL: J. Immunol. (Journal of Immunology) DATE: 2007 VOLUME: 178  
NUMBER: 4 PAGES: 2396-2406 CODEN: JOIMAS ISSN: 0022-1767 LANGUAGE:  
English PUBLISHER: American Association of Immunologists

6/3, K/8 (Item 4 from file: 399)  
DIALOG(R) File 399: CA SEARCH(R)  
(c) 2009 American Chemical Society. All rights reserved.

141230412 CA: 141(14)230412v JOURNAL  
Archaeosomes as Self-adjuvanting Delivery Systems for Cancer Vaccines  
AUTHOR(S): Krishnan, Lakshmi; Sprott, G. Dennis  
LOCATION: Inst. Biol. Sci., Natl. Res. Council Canada, Ottawa, ON, Can.,  
K1A 0R6  
JOURNAL: J. Drug Targeting (Journal of Drug Targeting) DATE: 2003  
VOLUME: 11 NUMBER: 8-10 PAGES: 515-524 CODEN: JDTAEH ISSN: 1061-186X  
LANGUAGE: English PUBLISHER: Taylor & Francis Ltd.

6/3, K/9 (Item 5 from file: 399)  
DIALOG(R) File 399: CA SEARCH(R)  
(c) 2009 American Chemical Society. All rights reserved.

141155579 CA: 141(10)155579z JOURNAL  
Archaeobacterial ether lipid liposomes as vaccine adjuvants  
AUTHOR(S): Sprott, G. Dennis; Patel, Girishchandra B.; Krishnan, Lakshmi  
LOCATION: Institute for Biological Sciences, National Research Council of  
Canada, Ottawa, ON, Can., K1A 0R6  
JOURNAL: Methods Enzymol. (Methods in Enzymology) DATE: 2003 VOLUME:  
373 NUMBER: Liposomes, Part C PAGES: 155-172 CODEN: MENZAU ISSN:  
0076-6879 LANGUAGE: English PUBLISHER: Elsevier

6/3, K/10 (Item 6 from file: 399)  
DIALOG(R) File 399: CA SEARCH(R)  
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139394847 CA: 139(26)394847a JOURNAL  
Archaeosomes varying in lipid composition differ in receptor-mediated  
endocytosis and differentially adjuvant immune responses to entrapped  
antigen  
AUTHOR(S): Sprott, G. Dennis; Sad, Subash; Fleming, L. Perry; Dicaire,  
Chantal J.; Patel, Girishchandra B.; Krishnan, Lakshmi  
LOCATION: Institute for Biological Sciences, National Research Council,  
Ottawa, ON, Can., K1A 0R6  
JOURNAL: Archaea (Archaea) DATE: 2003 VOLUME: 1 NUMBER: 3 PAGES:  
151-164 CODEN: ARCHCI ISSN: 1472-3646 LANGUAGE: English PUBLISHER:  
Heron Publishing

6/3, K/11 (Item 7 from file: 399)  
DIALOG(R) File 399: CA SEARCH(R)  
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139115967 CA: 139(8)115967b JOURNAL  
Archaeosomes Induce Enhanced Cytotoxic T Lymphocyte Responses to  
Page 25

10563731a.txt

Entrapped Soluble Protein in the Absence of Interleukin 12 and Protect  
against Tumor Challenge

AUTHOR(S): Krishnan, Lakshmi; Sad, Subash; Patel, Grishchandra B.;  
Sprott, G Dennis

LOCATION: Institute for Biological Sciences, National Research Council of  
Canada, Ottawa, ON, Can. K1A 0R6

JOURNAL: Cancer Res. (Cancer Research) DATE: 2003 VOLUME: 63 NUMBER:

10 PAGES: 2526-2534 CODEN: CNREAS ISSN: 0008-5472 LANGUAGE: English

PUBLISHER: American Association for Cancer Research

6/3, K/12 (Item 8 from file: 399)

DI ALOC(R) File 399: CA SEARCH(R)

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138152262 CA: 138(11)152262t PATENT

Vaccine adjuvant properties of liposomes formed at elevated temperatures  
from the polar chloroform extractable lipids from Mycobacterium bovis BCG  
INVENTOR(AUTHOR): Sprott, G Dennis; Krishnan, Lakshmi; Sad, Subash

LOCATION: Can.,

ASSIGNEE: National Research Council of Canada

PATENT: PCT International; WO 200311336 A2 DATE: 20030213

APPLICATI ON: WO 2002CA1217 (20020802) \*US PV309512 (20010803)

PAGES: 46 pp. CODEN: PIXXD2 LANGUAGE: English

PATENT CLASSIFI CATIONS:

CLASS: A61K-039/39A; A61K-009/127B; A61P-037/04B; A61P-035/00B

DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ;  
CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH;  
GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU;  
LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SD; SE;  
SG; SI; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZM; ZW  
AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW  
; MZ; SD; SL; SZ; TZ; UG; ZM; ZW AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES;  
FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; SK; TR; BF; BJ; CF; CG; CI; CM;  
GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG

6/3, K/13 (Item 9 from file: 399)

DI ALOC(R) File 399: CA SEARCH(R)

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134294515 CA: 134(21)294515u PATENT

Archaeosomes as immunomodulating carriers for acellular vaccines to  
induce cytotoxic T lymphocyte (CTL) responses and protect the vaccinated  
host against intracellular pathogens and cancer

INVENTOR(AUTHOR): Sprott, G Dennis; Krishnan, Lakshmi; Conlan, J. Wayne;  
Omri, Abdel; Patel, Grishchandra B.

LOCATION: Can.,

ASSIGNEE: National Research Council of Canada

PATENT: PCT International; WO 200126683 A2 DATE: 20010419

APPLICATI ON: WO 2000CA1197 (20001012) \*US PV158944 (19991012) \*US  
PV209988 (20000608)

PAGES: 98 pp. CODEN: PIXXD2 LANGUAGE: English

PATENT CLASSIFI CATIONS:

CLASS: A61K-039/39A; A61K-039/00B; A61K-039/02B; A61K-009/127B;

A61P-031/04B; A61P-031/12B; A61P-035/00B

DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ;  
CA; CH; CN; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR;  
HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA;  
MD; MG; MK; MN; MW; MX; MZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL;  
TJ; TM; TR; TT; TZ; UA; UG; UZ; VN; YU; ZA; ZW AM; AZ; BY; KG; KZ; MD; RU;  
TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZW  
; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE;

BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

6/3, K/14 (Item 10 from file: 399)

DI ALCOG R) File 399: CA SEARCH R)

(c) 2009 American Chemical Society. All rts. reserv.

134251017 CA: 134(18)251017r JOURNAL

The potent adjuvant activity of archaeosomes correlates to the recruitment and activation of macrophages and dendritic cells in vivo  
AUTHOR(S): Krishnan, Lakshmi; Sad, Subash; Patel, Grishchandra B.;

Spratt, G. Dennis

LOCATION: Institute for Biological Sciences, National Research Council of Canada, Ottawa, ON, Can., K1A 0R6

JOURNAL: J. Immunol. DATE: 2001 VOLUME: 166 NUMBER: 3 PAGES: 1885-1893 CODEN: JOIM33 ISSN: 0022-1767 LANGUAGE: English PUBLISHER: American Association of Immunologists

6/3, K/15 (Item 11 from file: 399)

DI ALCOG R) File 399: CA SEARCH R)

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132136166 CA: 132(11)136166k JOURNAL

Archaeosome vaccine adjuvants induce strong humoral, cell-mediated, and memory responses: comparison to conventional liposomes and alum

AUTHOR(S): Krishnan, Lakshmi; Dicaire, Chantal J.; Patel, Grishchandra B.; Spratt, G. Dennis

LOCATION: Institute for Biological Sciences, National Research Council of Canada, Ottawa, ON, Can., K1A 0R6

JOURNAL: Infect. Immun. DATE: 2000 VOLUME: 68 NUMBER: 1 PAGES: 54-63 CODEN: INFI3R ISSN: 0019-9567 LANGUAGE: English PUBLISHER: American Society for Microbiology

6/3, K/16 (Item 1 from file: 91)

DI ALCOG R) File 91: MANTIS TM

2001 (c) Action Potential. All rts. reserv.

00268401

Development of viper-venom antibodies in chicken egg yolk and assay of their antigen binding capacity.

MAYA DEVI, C.; VASANTHA BAI, M.; KRISHNAN, L. K.;

TOXICON. July 2002 (20020700), Vol 40, pp 857-61

ISSN: 0041-0101

MAYA DEVI, C.; VASANTHA BAI, M.; KRISHNAN, L. K.;

...from eggs. The isolation is very simple and involves only two steps, namely, removal of lipids from the diluted egg yolk followed by gel filtration. Each egg produces 80-100mg of...

6/3, K/17 (Item 1 from file: 149)

DI ALCOG R) File 149: TGG Health &amp; Wellness DB(SM)

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03115914 SUPPLIER NUMBER: 158235080 (USE FORMAT 7 OR 9 FOR FULL TEXT)

Adult stem cell homing and differentiation in vitro on composite fibrin matrix. (Author abstract)

Sreerekha, P. R.; Divya, P.; Krishnan, L. K.

Cell Proliferation, 39, 4, 301(12)

August,

2006

DOCUMENT TYPE: Author abstract PUBLICATION FORMAT: Magazine/ Journal

ISSN: 0960-7722 LANGUAGE: English RECORD TYPE: Abstract

TARGET AUDIENCE: Academic

... Krishnan, L. K.

...AUTHOR ABSTRACT: mRNA for and immunostaining the cells for von Willebrand factor, uptake of acetylated low-density lipoproteins and measurement of released nitric oxide in the culture medium as nitrite. The specific molecules...

? e au=sad, subash?

Ref	Items	Index-term
E1	1	AU=SAD, SAUM TRA
E2	76	AU=SAD, SUBASH
E3	0	*AU=SAD, SUBASH?
E4	2	AU=SAD, IA
E5	1	AU=SAD YKHOV, F. S.
E6	32	AU=SADA
E7	98	AU=SADA A
E8	4	AU=SADA A I
E9	2	AU=SADA A K A
E10	3	AU=SADA A M
E11	69	AU=SADA A
E12	1	AU=SADA AI

Enter P or PAGE for more

? s e1-e3

1	AU=SAD, SAUM TRA
76	AU=SAD, SUBASH
0	AU=SAD, SUBASH?
77	E1-E3

? rd

&gt;&gt;&gt;Duplicate detection is not supported for File 393.

&gt;&gt;&gt;Duplicate detection is not supported for File 391.

&gt;&gt;&gt;Records from unsupported files will be retained in the RD set.

S8 54 RD (unique items)

? t s8/3, k/1-54

&gt;&gt;&gt;KWC option is not available in file(s): 399

8/3, K/1 (Item 1 from file: 24)

DI ALCG(R) File 24: CSA Life Sciences Abstracts

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0003248421 I/P ACCESSION NO: 8201012

Pathogen Proliferation Governs the Magnitude but Compromises the Function of CD8 T Cells

Sad, Subash; Dudani, Renu; Qurnani, Komal; Russell, Marsha; van Faassen, Henk; Finlay, Brett; Krishnan, Lakshmi  
National Research Council-Institute for Biological Sciences, Ottawa,  
Ontario. Department of Biochemistry, Microbiology and Immunology,  
University of Ottawa, Ottawa, Ontario. Department of Microbiology and  
Immunology, University of British Columbia, Vancouver, British Columbia,  
Canada

Journal of Immunology, v 180, n 9, p 5853-5861, May 1, 2008

Page 28

PUBLICATION DATE: 2008

PUBLISHER: American Association of Immunologists, 9650 Rockville Pike  
Bethesda MD 20814-3998 USA, [URL: <http://www.jimmunol.org/>]

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0022-1767

ELECTRONIC ISSN: 1550-6606

FILE SEGMENT: Bacteriology Abstracts (Microbiology B); Immunology Abstracts

Sad, Subash; Dudani, Renu; Gurnani, Komal; Russell, Marsha; van  
Faassen, Henk; Finlay, Brett; Krishnan, Lakshmi8/3, K/2 (Item 2 from file: 24)  
DI ALCOG R File 24: CSA Life Sciences Abstracts  
(c) 2009 CSA. All rights reserved.0003182065 IP ACCESSION NO: 8039705  
Mutation in the Fas Pathway Impairs CD8 super(+) T Cell MemoryDudani, Renu; Russell, Marsha; van Faassen, Henk; Krishnan, Lakshmi;  
Sad, Subash  
National Research Council of Canada, Institute for Biological Sciences,  
Ottawa, Ontario, CanadaJournal of Immunology, v 180, n 5, p 2933-2941, March 1, 2008  
PUBLICATION DATE: 2008PUBLISHER: American Association of Immunologists, 9650 Rockville Pike  
Bethesda MD 20814-3998 USA, [URL: <http://www.jimmunol.org/>]

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0022-1767

FILE SEGMENT: Immunology Abstracts

Dudani, Renu; Russell, Marsha; van Faassen, Henk; Krishnan, Lakshmi;  
Sad, Subash8/3, K/3 (Item 3 from file: 24)  
DI ALCOG R File 24: CSA Life Sciences Abstracts  
(c) 2009 CSA. All rights reserved.0003114700 IP ACCESSION NO: 7743355  
Pregnancy Impairs the Innate Immune Resistance to Salmonella typhimurium  
Leading to Rapid Fatal InfectionPejčic-Karapetrovic, Branka; Gurnani, Komal; Russell, Marsha S; Finlay,  
BBrett; Sad, Subash; Krishnan, Lakshmi  
National Research Council-Institute for Biological Sciences, Ottawa,  
Ontario, Canada. Department of Biochemistry, Microbiology, and Immunology,  
University of Ottawa, Ottawa, Ontario, Canada. Michael Smith Laboratories,  
University of British Columbia, Vancouver, British Columbia, CanadaJournal of Immunology, v 179, n 9, p 6088-6096, November 1, 2007  
PUBLICATION DATE: 2007

10563731a.txt

PUBLISHER: American Association of Immunologists, 9650 Rockville Pike  
Bethesda MD 20814-3998 USA, [URL: <http://www.jimmunol.org/>]

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0022-1767

FILE SEGMENT: Bacteriology Abstracts (Microbiology B); Immunology Abstracts

Pejčić-Karapetrović, Branka; Gurnani, Komal; Russell, Marsha S; Finlay, BBrett; Sad, Subash; Krishnan, Lakshmi

8/3, K/4 (Item 4 from file: 24)

DI ALCOG R File 24: CSA Life Sciences Abstracts

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0003014138 IP ACCESSION NO: 7289082

Rapid Clonal Expansion and Prolonged Maintenance of Memory CD8 super(+) T Cells of the Effector (CD44 super(high) CD62L super(low)) and Central (CD44 super(high) CD62L super(high)) Phenotype by an Archaeosome Adjuvant Independent of TLR2

Krishnan, Lakshmi; Gurnani, Komal; Dicairé, Chantal J; van Faassen, Henk; Zafer, Ahmed; Kirschning, Carsten J; Sad, Subash; Sprött, Gdennis

National Research Council-Institute for Biological Sciences, Ottawa, Ontario, Canada, Department of Biochemistry, Microbiology, and Immunology, University of Ottawa, Ottawa, Ontario, Canada, Institute for Microbiology, Immunology, and Hygiene, Technical University, Munich, Germany

Journal of Immunology, v 178, n 4, p 2396-2406, February 2007

PUBLICATION DATE: 2007

PUBLISHER: American Association of Immunologists, 9650 Rockville Pike  
Bethesda MD 20814-3998 USA, [URL: <http://www.jimmunol.org/>]

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0022-1767

FILE SEGMENT: Bacteriology Abstracts (Microbiology B); Immunology Abstracts

Krishnan, Lakshmi; Gurnani, Komal; Dicairé, Chantal J; van Faassen, Henk; Zafer, Ahmed; Kirschning, Carsten J; Sad, Subash; Sprött, Gdennis

8/3, K/5 (Item 5 from file: 24)

DI ALCOG R File 24: CSA Life Sciences Abstracts

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0002984978 IP ACCESSION NO: 7129075

Delayed Expansion and Contraction of CD8 super(+) T Cell Response during Infection with Virulent Salmonella typhimurium

Luu, Rachel A; Gurnani, Komal; Dudani, Renu; Karmara, Rajagopal; van Faassen, Henk; Sirard, Jean-Claude; Krishnan, Lakshmi; Sad, Subash; Laboratory of Cellular Immunology, National Research Council-Institute for Biological Sciences, Ottawa, Canada, Institut National de la Santé et de la Recherche Médicale, Institut de Biologie, Campus Pasteur Lille, Lille,

10563731a.txt

France. Department of Biochemistry, Microbiology, and Immunology,  
University of Ottawa, Ontario, Canada

Journal of Immunology, v 177, n 3, p 1516-1525, August 1, 2006  
PUBLICATION DATE: 2006

PUBLISHER: American Association of Immunologists, 9650 Rockville Pike  
Bethesda MD 20814-3998 USA, [URL: <http://www.jimmunol.org/>]

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0022-1767

FILE SEGMENT: Bacteriology Abstracts (Microbiology B); Immunology Abstracts

...A; Gurnani, Komal; Dudani, Penu; Kamra, Rajagopal; van Faassen,  
Henk; Sirard, Jean-Claude; Krishnan, Lakshmi; Sad, Subash

8/3, K/6 (Item 6 from file: 24)

DIALOG(R) File 24: CSA Life Sciences Abstracts

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0002841244 IP ACCESSION NO: 6932929

Apoptotic Vesicles Crossprime CD8 T Cells and Protect against Tuberculosis

Wnau, Florian; Weber, Stephan; Sad, Subash; De Diego, Juana;  
Hoops, Silvia Locatelli; Breiden, Bernadette; Sandhoff, Konrad;  
Brinkmann, Volker; Kaufmann, Stefan HE; Schaible, Ulrich E  
Department of Immunology, Max-Planck-Institute for Infection Biology,  
Schumannstrasse 21-22, 10117 Berlin, Germany,  
[mailto:wnau@mpiib-berlin.mpg.de]

Immunity, v 24, n 1, p 105-117, 2006

PUBLICATION DATE: 2006

PUBLISHER: Cell Press, 1100 Massachusetts Avenue Cambridge MA 02138 USA,  
[mailto:subs@cell.com], [URL: <http://www.cellpress.com/>]

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 1074-7613

FILE SEGMENT: Bacteriology Abstracts (Microbiology B); Immunology Abstracts

Wnau, Florian; Weber, Stephan; Sad, Subash; De Diego, Juana;  
Hoops, Silvia Locatelli; Breiden, Bernadette; Sandhoff, Konrad;  
Brinkmann, Volker; Kaufmann, Stefan...

8/3, K/7 (Item 7 from file: 24)

DIALOG(R) File 24: CSA Life Sciences Abstracts

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0002800467 IP ACCESSION NO: 6662144

Impaired Protection against Mycobacterium bovis Bacillus Calmette-Guérin  
Infection in IL-15-Deficient Mice

Saito, Kimika; Yajima, Toshiki; Kumabe, Shino; Doi, Takehiko; Yamada,  
Hisakata; Sad, Subash; Shen, Hao; Yoshikai, Yasunobu  
Division of Host Defense, Medical Institute of Bioregulation, Kyushu

10563731a.txt

University, Fukuoka, Japan. Laboratory of Cellular Immunology, Institute for Biological Sciences, National Research Council of Canada, Ottawa, Ontario, Canada. Department of Microbiology, School of Medicine, University of Pennsylvania, Philadelphia, PA 19104

Journal of Immunology, v 176, n 4, p 2496-2504, February 2006  
PUBLICATION DATE: 2006

PUBLISHER: American Association of Immunologists, 9650 Rockville Pike  
Bethesda MD 20814-3998 USA, [URL: <http://www.jimmunol.org/>]

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0022-1767

FILE SEGMENT: Immunology Abstracts; Bacteriology Abstracts (Microbiology B)

Saito, Kimika; Yajima, Toshiaki; Kumabe, Shino; Doi, Takehiko; Yamada, Hisakata; Sad, Subash; Shen, Hao; Yoshikai, Yasunobu

8/3, K/8 (Item 8 from file: 24)  
DIALOG(R) File 24: CSA Life Sciences Abstracts  
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0002779077 IP ACCESSION NO: 6577999  
IL-15 Regulates CD8 super(+) T Cell Contraction during Primary Infection

Yajima, Toshiaki; Yoshihara, Kazufumi; Nakazato, Kenji; Kumabe, Shino; Koyasu, Shigeo; Sad, Subash; Shen, Hao; Kuwano, Hiroyuki; Yoshikai, Yasunobu  
Division of Host Defense, Medical Institute of Bioregulation, Kyushu University, Fukuoka, Japan. First Department of Surgery, Gunma University School of Medicine, Maebashi, Japan. Department of Microbiology and Immunology, Keio University School of Medicine, Tokyo, Japan. Laboratory of Cellular Immunology, Institute for Biological Sciences, National Research Council of Canada, Ottawa, Canada. Department of Microbiology, School of Medicine, University of Pennsylvania, Philadelphia PA 19104

Journal of Immunology, v 176, n 1, p 507-515, January 1, 2006  
PUBLICATION DATE: 2006

PUBLISHER: American Association of Immunologists, 9650 Rockville Pike  
Bethesda MD 20814-3998 USA, [URL: <http://www.jimmunol.org/>]

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0022-1767

FILE SEGMENT: Immunology Abstracts

Yajima, Toshiaki; Yoshihara, Kazufumi; Nakazato, Kenji; Kumabe, Shino; Koyasu, Shigeo; Sad, Subash; Shen, Hao; Kuwano, Hiroyuki; Yoshikai, Yasunobu

8/3, K/9 (Item 9 from file: 24)  
DIALOG(R) File 24: CSA Life Sciences Abstracts  
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0002723132 IP ACCESSION NO: 6275568  
Page 32

10563731a.txt

Reducing the Stimulation of CD8 super(+) T Cells during Infection with Intracellular Bacteria Promotes Differentiation Primarily into a Central (CD62L super(hi gh) CD44 super(hi gh)) Subset

van Faassen, Henk; Saldanha, Marsha; Gilbertson, Deanna; Dudani, Renu; Krishnan, Lakshmi; Sad, Subash  
Laboratory of Cellular Immunology, Institute for Biological Sciences,  
National Research Council of Canada, Ottawa, Ontario, Canada

Journal of Immunology, v 174, n 9, p 5341-5350, May 1, 2005

PUBLICATION DATE: 2005

PUBLISHER: American Association of Immunologists, 9650 Rockville Pike  
Bethesda MD 20814-3998 USA, [URL: <http://www.jimmunol.org/>]

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0022-1767

FILE SEGMENT: Immunology Abstracts

van Faassen, Henk; Saldanha, Marsha; Gilbertson, Deanna; Dudani, Renu;  
Krishnan, Lakshmi; Sad, Subash

8/3, K/10 (Item 10 from file: 24)

DIALOG(R) File 24: CSA Life Sciences Abstracts

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0002664024 IP ACCESSION NO: 6190482

A Novel Role of IL-15 in Early Activation of Memory CD8 super(+) CTL after Re-infection

Yajima, Toshiaki; Nishimura, Hitoshi; Sad, Subash; Shen, Hao;  
Kuwano, Hiroyuki; Yoshikai, Yasunobu  
Division of Host Defense, Medical Institute of Bioregulation, Kyushu  
University, Fukuoka, Japan

Journal of Immunology, v 174, n 6, p 3590-3597, March 15, 2005

PUBLICATION DATE: 2005

PUBLISHER: American Association of Immunologists, 9650 Rockville Pike  
Bethesda MD 20814-3998 USA, [URL: <http://www.jimmunol.org/>]

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0022-1767

FILE SEGMENT: Immunology Abstracts; Bacteriology Abstracts (Microbiology B)

Yajima, Toshiaki; Nishimura, Hitoshi; Sad, Subash; Shen, Hao;  
Kuwano, Hiroyuki; Yoshikai, Yasunobu

8/3, K/11 (Item 11 from file: 24)

DIALOG(R) File 24: CSA Life Sciences Abstracts

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0002606667 IP ACCESSION NO: 5992116

Activation of Dendritic Cells by Liposomes Prepared from  
Phosphatidyl inositol Mannosides from Mycobacterium bovis Bacillus Calmette-  
Guerin and Adjuvant Activity In Vivo

Sprott, GDennis; Dicaire, Chantal J; Gurnani, Komal; Sad, Subash;  
Krishnan, Lakshmi  
Institute for Biological Sciences, National Research Council, Ottawa,  
Ontario, Canada

Infection and Immunity, v 72, n 9, p 5235-5246, September 2004  
PUBLICATION DATE: 2004

PUBLISHER: American Society for Microbiology, 1752 N Street N.W  
Washington, DC 20036 USA, [URL: <http://www.asn.org/>]

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ISSN: 0019-9567  
FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

Sprott, GDennis; Dicaire, Chantal J; Gurnani, Komal; Sad, Subash;  
Krishnan, Lakshmi

8/3, K/12 (Item 12 from file: 24)  
DIALOG File 24: CSA Life Sciences Abstracts  
(c) 2009 CSA. All rights reserved.

0002592371 IP ACCESSION NO: 5946009  
Phosphatidylserine Receptor-Mediated Recognition of Archaeosome Adjuvant  
Promotes Endocytosis and MHC Class II Cross-Presentation of the Entrapped  
Antigen by Phagosome-to-Cytosol Transport and Classical Processing

Gurnani, Komal; Kennedy, Jessica; Sad, Subash; Sprott, GDennis;  
Krishnan, Lakshmi  
National Research Council of Canada, Institute for Biological Sciences,  
Ottawa, Ontario, Canada

Journal of Immunology, v 173, n 1, p 566-578, July 1, 2004  
PUBLICATION DATE: 2004

PUBLISHER: American Association of Immunologists, 9650 Rockville Pike  
Bethesda MD 20814-3998 USA, [URL: <http://www.jimmunol.org/>]

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ISSN: 0022-1767  
FILE SEGMENT: Immunology Abstracts

Gurnani, Komal; Kennedy, Jessica; Sad, Subash; Sprott, GDennis;  
Krishnan, Lakshmi

8/3, K/13 (Item 1 from file: 41)  
DIALOG File 41: Pollution Abstracts  
(c) 2009 CSA. All rights reserved.

0000311396 IP ACCESSION NO: 7463375  
A Reduced Antigen Load In Vivo, Rather Than Weak Inflammation, Causes a  
Substantial Delay in CD8 super(+) T Cell Priming against Mycobacterium  
bovis (Bacillus Calmette-Guérin)

10563731a.txt

Russell, Marsha S; Iskandar, Monica; Myktyczuk, Oksana L; Nash, John HE;  
Krishnan, Lakshmi; Sad, Subash  
National Research Council-Institute for Biological Sciences and Department  
of Biochemistry, Microbiology, and Immunology, University of Ottawa,  
Ottawa, Ontario, Canada

Journal of Immunology, v 179, n 1, p 211-220, July 1, 2007

PUBLICATION DATE: 2007

PUBLISHER: American Association of Immunologists, 9650 Rockville Pike  
Bethesda MD 20814-3998 USA, [URL: <http://www.jimmunol.org/>]

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0022-1767

Russell, Marsha S; Iskandar, Monica; Myktyczuk, Oksana L; Nash, John HE;  
Krishnan, Lakshmi; Sad, Subash

8/3, K/14 (Item 1 from file: 143)  
DIALCOG(R) File 143: Biol. & Agric. Index  
(c) 2009 The HW Wilson Co. All rts. reserv.

1844483 H.W. WILSON RECORD NUMBER: BBAI 05117035  
A Novel Role of IL-15 in Early Activation of Memory CD8+ CTL after  
Reinfection  
Yajima, Toshiaki  
Nishimura, Hitoshi; Sad, Subash  
Journal of Immunology v. 174 no6 (March 15 2005) p. 3590-7  
ISSN: 0022-1767

...Sad, Subash

8/3, K/15 (Item 2 from file: 143)  
DIALCOG(R) File 143: Biol. & Agric. Index  
(c) 2009 The HW Wilson Co. All rts. reserv.

1306149 H.W. WILSON RECORD NUMBER: BBAI 01007647  
The potent adjuvant activity of archaeosomes correlates to the recruitment  
and activation of macrophages and dendritic cells in vivo  
Krishnan, Lakshmi  
Sad, Subash; Patel, B. Grishchandra  
Journal of Immunology v. 166 no3 (Feb. 1 2001) p. 1885-93  
DOCUMENT TYPE: Feature Article ISSN: 0022-1767

Sad, Subash...

8/3, K/16 (Item 3 from file: 143)  
DIALCOG(R) File 143: Biol. & Agric. Index  
(c) 2009 The HW Wilson Co. All rts. reserv.

1276814 H.W. WILSON RECORD NUMBER: BBAI 00061612  
Archaeosomes induce long-term CD8+ cytotoxic T cell response to entrapped  
soluble protein by the exogenous cytosolic pathway, in the absence of  
CD4+ T cell help  
Krishnan, Lakshmi  
Sad, Subash; Patel, Grishchandra B.  
Journal of Immunology v. 165 no9 (Nov. 1 2000) p. 5177-85

Sad, Subash...

8/3, K/17 (Item 4 from file: 143)  
 DIALOG(R) File 143: Biol. & Agric. Index  
 (c) 2009 The HW Wilson Co. All rts. reserv.

1116630 H.W. WILSON RECORD NUMBER: BBAI 99056974  
 Cytokine deprivation of naive CD8+ T cells promotes minimal cell cycling  
 but maximal cytokine synthesis and autonomous proliferation subsequently:  
 a mechanism of self-regulation

Sad, Subash

Krishnan, Lakshmi

Journal of Immunology v. 163 no5 (Sept. 1 1999) p. 2443-51

DOCUMENT TYPE: Feature Article ISSN: 0022-1767

Sad, Subash

8/3, K/18 (Item 5 from file: 143)  
 DIALOG(R) File 143: Biol. & Agric. Index  
 (c) 2009 The HW Wilson Co. All rts. reserv.

0735770 H.W. WILSON RECORD NUMBER: BBAI 97043159  
 Cytokine-deficient CD8+ Tc1 cells induced by IL-4. Retained inflammation  
 and perforin and Fas cytotoxicity but compromised long term killing of  
 tumor cells

Sad, Subash

Li, Li; Mbsmann, Tim R

Journal of Immunology v. 159 (July 15 '97) p. 606-13

DOCUMENT TYPE: Feature Article ISSN: 0022-1767

Sad, Subash

8/3, K/19 (Item 6 from file: 143)  
 DIALOG(R) File 143: Biol. & Agric. Index  
 (c) 2009 The HW Wilson Co. All rts. reserv.

0707466 H.W. WILSON RECORD NUMBER: BBAI 97029013  
 CD8Tc1 and Tc2 cells secrete distinct cytokine patterns in vitro and in  
 vivo but induce similar inflammatory reactions

Li, Li

Sad, Subash; Kagi, David

Journal of Immunology v. 158 (May 1 '97) p. 4152-61

DOCUMENT TYPE: Feature Article ISSN: 0022-1767

Sad, Subash...

8/3, K/20 (Item 7 from file: 143)  
 DIALOG(R) File 143: Biol. & Agric. Index  
 (c) 2009 The HW Wilson Co. All rts. reserv.

0687949 H.W. WILSON RECORD NUMBER: BBAI 94048220  
 Single IL-2-secreting precursor CD4 T cell can develop into either Th1 or  
 Th2 cytokine secretion phenotype

Sad, Subash

Mbsmann, Tim R

Journal of Immunology v. 153 (Oct. 15 '94) p. 3514-22

DOCUMENT TYPE: Feature Article ISSN: 0022-1767

Sad, Subash

8/3, K/21 (Item 1 from file: 399)  
 DI ALCOG R File 399: CA SEARCH(R)  
 (c) 2009 American Chemical Society. All rts. reserv.  
 151356301 CA: 151(16)356301h JOURNAL  
 Selectively Reduced Intracellular Proliferation of Salmonella enterica  
 Serovar Typhimurium within APCs Limits Antigen Presentation and  
 Development of a Rapid CD8 T Cell Response  
 AUTHOR(S): Albaghdadi, Homa; Robinson, Nirmal; Finlay, Brett; Krishnan,  
 Lakshmi; Sad, Subash  
 LOCATION: National Research Council Institute for Biological Sciences,  
 Ottawa, ON, Can.,  
 JOURNAL: J. Immunol. (Journal of Immunology) DATE: 2009 VOLUME: 183  
 NUMBER: 6 PAGES: 3778-3787 CODEN: JOIMAS ISSN: 0022-1767 LANGUAGE:  
 English PUBLISHER: American Association of Immunologists

8/3, K/22 (Item 2 from file: 399)  
 DI ALCOG R File 399: CA SEARCH(R)  
 (c) 2009 American Chemical Society. All rts. reserv.  
 151006435 CA: 151(1)6435d JOURNAL  
 Intracellular Bacterial Vectors That Induce CD8+ T Cells with Similar  
 Cytolytic Abilities but Disparate Memory Phenotypes Provide Contrasting  
 Tumor Protection  
 AUTHOR(S): Stark, Felicity C.; Sad, Subash; Krishnan, Lakshmi  
 LOCATION: Department of Biochemistry, Microbiology and Immunology,  
 University of Ottawa and National Research Council-Institute for Biological  
 Sciences, Ottawa, ON, Can.,  
 JOURNAL: Cancer Res. (Cancer Research) DATE: 2009 VOLUME: 69 NUMBER:  
 10 PAGES: 4327-4334 CODEN: CNREAS ISSN: 0008-5472 LANGUAGE: English  
 PUBLISHER: American Association for Cancer Research

8/3, K/23 (Item 3 from file: 399)  
 DI ALCOG R File 399: CA SEARCH(R)  
 (c) 2009 American Chemical Society. All rts. reserv.  
 149244073 CA: 149(11)244073n JOURNAL  
 IFN- $\gamma$  Induces the Erosion of Preexisting CD8 T Cell Memory during  
 Infection with a Heterologous Intracellular Bacterium  
 AUTHOR(S): Dudani, Renu; Murali-Krishna, Kaja; Krishnan, Lakshmi; Sad,  
 Subash  
 LOCATION: National Research Council-Institute for Biological Sciences,  
 Ottawa, ON, Can.,  
 JOURNAL: J. Immunol. (Journal of Immunology) DATE: 2008 VOLUME: 181  
 NUMBER: 3 PAGES: 1700-1709 CODEN: JOIMAS ISSN: 0022-1767 LANGUAGE:  
 English PUBLISHER: American Association of Immunologists

8/3, K/24 (Item 4 from file: 399)  
 DI ALCOG R File 399: CA SEARCH(R)  
 (c) 2009 American Chemical Society. All rts. reserv.  
 148469937 CA: 148(21)469937b JOURNAL  
 Mutation in the Fas Pathway Impairs CD8+ T Cell Memory  
 AUTHOR(S): Dudani, Renu; Russell, Marsha; van Faassen, Henk; Krishnan,  
 Lakshmi; Sad, Subash  
 LOCATION: National Research Council of Canada, Institute for Biological  
 Page 37

Sciences, Ottawa, ON, Can.,

JOURNAL: J. Immunol. (Journal of Immunology) DATE: 2008 VOLUME: 180  
NUMBER: 5 PAGES: 2933-2941 CODEN: JOIM33 ISSN: 0022-1767 LANGUAGE:  
English PUBLISHER: American Association of Immunologists

8/3, K/25 (Item 5 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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148305994 CA: 148(14)305994s CONFERENCE PROCEEDING

Antigen processing and presentation

AUTHOR(S): Sad, Subash

LOCATION: Institute for Biological Sciences, National Research Council of  
Canada, Ottawa, ON, Can.,

JOURNAL: Vaccine Adjuvants Delivery Syst. (Vaccine Adjuvants and Delivery  
Systems) EDITOR: Singh, Manmohan (Ed), DATE: 2007 PAGES: 33-52 CODEN:  
69KEQD LANGUAGE: English PUBLISHER: John Wiley & Sons, Inc., Hoboken, N. J

8/3, K/26 (Item 6 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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147070598 CA: 147(4)70598d JOURNAL

A Reduced Antigen Load In Vivo, Rather Than Weak Inflammation, Causes a  
Substantial Delay in CD8+ T Cell Priming against Mycobacterium bovis  
(Bacillus Calmette-Guérin)

AUTHOR(S): Russell, Marsha S.; Iskandar, Monica; Mykytczuk, Oksana L.;  
Nash, John H. E.; Krishnan, Lakshmi; Sad, Subash

LOCATION: National Research Council-Institute for Biological Sciences,  
University of Ottawa, Ottawa, ON, Can.,

JOURNAL: J. Immunol. (Journal of Immunology) DATE: 2007 VOLUME: 179  
NUMBER: 1 PAGES: 211-220 CODEN: JOIM33 ISSN: 0022-1767 LANGUAGE:  
English PUBLISHER: American Association of Immunologists

8/3, K/27 (Item 7 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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146204273 CA: 146(11)204273j JOURNAL

Rapid Clonal Expansion and Prolonged Maintenance of Memory CD8+ T Cells  
of the Effector (CD44hi ghCD62L low) and Central (CD44hi ghCD62L high)  
Phenotype by an Archaeosome Adjuvant Independent of TLR2

AUTHOR(S): Krishnan, Lakshmi; Gurnani, Komal; Dicaire, Chantal J.; van  
Faassen, Henk; Zafer, Ahmed; Kirschning, Carsten J.; Sad, Subash; Sprott,  
G. Dennis

LOCATION: Institute for Biological Sciences, National Research Council,  
Ottawa, ON, Can.,

JOURNAL: J. Immunol. (Journal of Immunology) DATE: 2007 VOLUME: 178  
NUMBER: 4 PAGES: 2396-2406 CODEN: JOIM33 ISSN: 0022-1767 LANGUAGE:  
English PUBLISHER: American Association of Immunologists

8/3, K/28 (Item 8 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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145122983 CA: 145(7)122983f JOURNAL

Delayed Expansion and Contraction of CD8+ T Cell Response during  
infection with Virulent Salmonella typhimurium

AUTHOR(S): Luu, Rachel A.; Gurnani, Komal; Dudani, Renu; Kamrara,

10563731a.txt

Rajagopal; van Faassen, Henk; Sirard, Jean-Claude; Krishnan, Lakshmi; Sad, Subash

LOCATION: Laboratory of Cellular Immunology, National Research Council-Institute for Biological Sciences, ON, Can.,

JOURNAL: J. Immunol. (Journal of Immunology) DATE: 2006 VOLUME: 177  
NUMBER: 3 PAGES: 1516-1525 CODEN: JOIM3 ISSN: 0022-1767 LANGUAGE: English PUBLISHER: American Association of Immunologists

8/3, K/29 (Item 9 from file: 399)

DI ALOG(R) File 399: CA SEARCH(R)

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144086336 CA: 144(6) 86336 JOURNAL

IL-15 Regulates CD8+ T Cell Contraction during Primary Infection

AUTHOR(S): Yajima, Toshiki; Yoshihara, Kazufumi; Nakazato, Kenji; Kurabe, Shino; Koyasu, Shigeo; Sad, Subash; Shen, Hao; Kuwano, Hiroyuki; Yoshikai, Yasunobu

LOCATION: Division of Host Defense, Medical Institute of Bioregulation, Kyushu University, Fukuoka, Japan, 812-8582

JOURNAL: J. Immunol. (Journal of Immunology) DATE: 2005 VOLUME: 176

NUMBER: 1 PAGES: 507-515 CODEN: JOIM3 ISSN: 0022-1767 LANGUAGE: English MEETING DATE: 20060000 PUBLISHER: American Association of Immunologists

8/3, K/30 (Item 10 from file: 399)

DI ALOG(R) File 399: CA SEARCH(R)

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140285850 CA: 140(18) 285850w JOURNAL

Prolonged Antigen Presentation, APC-, and CD8+ T Cell Turnover during Mycobacterial Infection: Comparison with *Listeria monocytogenes*

AUTHOR(S): van Faassen, Henk; Dudani, Penu; Krishnan, Lakshmi; Sad, Subash

LOCATION: Institute for Biological Sciences, Laboratory of Cellular Immunology, National Research Council of Canada, Ottawa, ON, Can.,

JOURNAL: J. Immunol. (Journal of Immunology) DATE: 2004 VOLUME: 172

NUMBER: 6 PAGES: 3491-3500 CODEN: JOIM3 ISSN: 0022-1767 LANGUAGE: English PUBLISHER: American Association of Immunologists

8/3, K/31 (Item 11 from file: 399)

DI ALOG(R) File 399: CA SEARCH(R)

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139394847 CA: 139(26) 394847a JOURNAL

Archaeosomes varying in lipid composition differ in receptor-mediated endocytosis and differentially adjuvant immune responses to entrapped antigen

AUTHOR(S): Sprott, G Dennis; Sad, Subash; Fleming, L. Perry; Di caire, Chantal J.; Patel, Girishchandra B.; Krishnan, Lakshmi

LOCATION: Institute for Biological Sciences, National Research Council, Ottawa, ON, Can., K1A 0R6

JOURNAL: Archaea (Archaea) DATE: 2003 VOLUME: 1 NUMBER: 3 PAGES: 151-164 CODEN: ARCH1 ISSN: 1472-3646 LANGUAGE: English PUBLISHER: Heron Publishing

8/3, K/32 (Item 12 from file: 399)

DI ALOG(R) File 399: CA SEARCH(R)

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139394612 CA: 139(26)394612v JOURNAL  
Increased CD8+ T Cell Memory to Concurrent Infection at the Expense of  
Increased Erosion of Pre-existing Memory: The Paradoxical Role of IL-15  
AUTHOR(S): Chapdelaine, Yvan; Smith, Dean K.; Pedras-Vasconcelos, Joao A.  
; Krishnan, Lakshmi; Sad, Subash  
LOCATION: Institute for Biological Sciences, Laboratory of Cellular  
Immunology, National Research Council of Canada, Ottawa, ON, Can., K1A 0R6  
JOURNAL: J. Immunol. (Journal of Immunology) DATE: 2003 VOLUME: 171  
NUMBER: 10 PAGES: 5454-5460 CODEN: JOIMAS ISSN: 0022-1767 LANGUAGE:  
English PUBLISHER: American Association of Immunologists

8/3, K/33 (Item 13 from file: 399)  
DI ALCG(R) File 399: CA SEARCH(R)  
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139290659 CA: 139(19)290659z JOURNAL  
Maintenance and attrition of T-cell memory  
AUTHOR(S): Sad, Subash; Krishnan, Lakshmi  
LOCATION: Institute for Biological Sciences, National Research Council of  
Canada, Ottawa, ON, Can.,  
JOURNAL: Crit. Rev. Immunol. (Critical Reviews in Immunology) DATE: 2003  
VOLUME: 23 NUMBER: 1 & 2 PAGES: 129-147 CODEN: OCRI DE ISSN: 1040-8401  
LANGUAGE: English PUBLISHER: Begell House, Inc.

8/3, K/34 (Item 14 from file: 399)  
DI ALCG(R) File 399: CA SEARCH(R)  
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139115967 CA: 139(8)115967b JOURNAL  
Archaeosomes Induce Enhanced Cytotoxic T Lymphocyte Responses to  
Entrapped Soluble Protein in the Absence of Interleukin 12 and Protect  
against Tumor Challenge  
AUTHOR(S): Krishnan, Lakshmi; Sad, Subash; Patel, Girishchandra B.;  
Sprott, G. Dennis  
LOCATION: Institute for Biological Sciences, National Research Council of  
Canada, Ottawa, ON, Can., K1A 0R6  
JOURNAL: Cancer Res. (Cancer Research) DATE: 2003 VOLUME: 63 NUMBER:  
10 PAGES: 2526-2534 CODEN: CNREAS ISSN: 0008-5472 LANGUAGE: English  
PUBLISHER: American Association for Cancer Research

8/3, K/35 (Item 15 from file: 399)  
DI ALCG(R) File 399: CA SEARCH(R)  
(c) 2009 American Chemical Society. All rts. reserv.

139067771 CA: 139(5)67771j PATENT  
Differential induction, maintenance and regulation of CD8+ T cell  
response against a model antigen expressed by an acute versus a chronic  
intracellular bacterium  
INVENTOR(AUTHOR): Sad, Subash; Chapdelaine, Yvan; Smith, Dean K.; Dudani,  
Renu  
LOCATION: Can.,  
ASSIGNEE: National Research Council of Canada  
PATENT: PCT International ; WO 200353459 A2 DATE: 20030703  
APPLICATION: WO 2002CA1892 (20021210) \*US PV337146 (20011210)  
PAGES: 36 pp. CODEN: PIXD2 LANGUAGE: English  
PATENT CLASSIFICATIONS:

CLASS: A61K-038/20A; A61K-038/17B; A61K-035/74B  
DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ;  
CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH;  
GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KZ; LC; LK; LR; LS; LT; LU;

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LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RQ; RU; SC; SD;  
SE; SG; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZM;  
ZW AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS;  
; MW; MZ; SD; SL; SZ; TZ; UG; ZM; ZW AT: BE; BG; CH; CY; CZ; DE; DK; EE;  
ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; SI; SK; TR; BF; BJ; CF; CG;  
CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG

8/3, K/36 (Item 16 from file: 399)

DI ALCOG R File 399: CA SEARCH R

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138152262 CA: 138(11)152262 PATENT

Vaccine adjuvant properties of liposomes formed at elevated temperatures  
from the polar chloroform extractable lipids from *Mycobacterium bovis* BCG  
INVENTOR(AUTHOR): Sprott, G Dennis; Krishnan, Lakshmi; Sad, Subash

LOCATION: Can.,

ASSIGNEE: National Research Council of Canada

PATENT: PCT International; WO 200311336 A2 DATE: 20030213

APPLICATI ON: WO 2002CA1217 (20020802) \*US PV309512 (20010803)

PAGES: 46 pp. CODEN: PIXD2 LANGUAGE: English

PATENT CLASSIFI CATIONS:

CLASS: A61K-039/39A; A61K-009/127B; A61P-037/04B; A61P-035/00B

DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ;  
CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH;  
GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU;  
LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RQ; RU; SD; SE;  
SG; SI; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZM; ZW  
AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW;  
; MZ; SD; SL; SZ; TZ; UG; ZM; ZW AT: BE; BG; CH; CY; CZ; DE; DK; EE; ES;  
FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; SK; TR; BF; BJ; CF; CG; CI; CM;  
GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG

8/3, K/37 (Item 17 from file: 399)

DI ALCOG R File 399: CA SEARCH R

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137167890 CA: 137(12)167890 JOURNAL

Cross-reactive antigen is required to prevent erosion of established T  
cell memory and tumor immunity: a heterologous bacterial model of  
attrition

AUTHOR(S): Smith, Dean K; Dudani, Renu; Pedras-Vasconcelos, Joao A;  
Chappelaine, Yvan; Van Faassen, Henk; Sad, Subash

LOCATION: Laboratory of Cellular Immunology, Institute for Biological  
Sciences, National Research Council, Ottawa, ON, Can.,

JOURNAL: J. Immunol. (Journal of Immunology) DATE: 2002 VOLUME: 169

NUMBER: 3 PAGES: 1197-1206 CODEN: JOIM3 ISSN: 0022-1767 LANGUAGE:

English PUBLISHER: American Association of Immunologists

8/3, K/38 (Item 18 from file: 399)

DI ALCOG R File 399: CA SEARCH R

(c) 2009 American Chemical Society. All rts. reserv.

137139243 CA: 137(10)139243 JOURNAL

*Mycobacterium bovis* BCG-infected mice are more susceptible to  
staphylococcal enterotoxin B-mediated toxic shock than uninfected mice  
despite reduced in vitro splenocyte responses to superantigens

AUTHOR(S): Pedras-Vasconcelos, Joao A; Chappelaine, Yvan; Dudani, Renu;  
Van Faassen, Henk; Smith, Dean K; Sad, Subash

LOCATION: Laboratory of Cellular Immunology, Institute for the Biological  
Sciences, National Research Council, Ottawa, ON, Can., K1A 0P6

10563731a.txt

JOURNAL: Infect. Immun. (Infection and Immunity) DATE: 2002 VOLUME: 70  
NUMBER: 8 PAGES: 4148-4157 CODEN: INFI BR ISSN: 0019-9567 LANGUAGE:  
English PUBLISHER: American Society for Microbiology

8/3, K/39 (Item 19 from file: 399)

DI ALCO R File 399: CA SEARCH R

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137062116 CA: 137(5)62116y JOURNAL

Multiple mechanisms compensate to enhance tumor-protective CD8+ T cell  
response in the long-term despite poor CD8+ T cell priming initially:  
comparison between an acute versus a chronic intracellular bacterium  
expressing a model antigen

AUTHOR(S): Dudani, Penu; Chapdelaine, Yvan; Van Faassen, Henk; Smith,  
Dean K.; Shen, Hao; Krishnan, Lakshmi; Sad, Subash

LOCATION: Laboratory of Cellular Immunology, Institute for Biological  
Sciences, National Research Council, Ottawa, ON, Can., K1A 0R6

JOURNAL: J. Immunol. (Journal of Immunology) DATE: 2002 VOLUME: 168

NUMBER: 11 PAGES: 5737-5745 CODEN: JOIM A3 ISSN: 0022-1767 LANGUAGE:  
English PUBLISHER: American Association of Immunologists

8/3, K/40 (Item 20 from file: 399)

DI ALCO R File 399: CA SEARCH R

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136339120 CA: 136(22)339120w JOURNAL

Preexisting inflammation due to Mycobacterium bovis BCG infection  
differentially modulates T-cell priming against a replicating or  
nonreplicating immunogen

AUTHOR(S): Dudani, Penu; Chapdelaine, Yvan; Van Faassen, Henk; Smith,  
Dean K.; Shen, Hao; Krishnan, Lakshmi; Sad, Subash

LOCATION: Laboratory of Cellular Immunology, Institute for Biological  
Sciences, National Research Council, Ottawa, ON, Can., K1A 0R6

JOURNAL: Infect. Immun. DATE: 2002 VOLUME: 70 NUMBER: 4 PAGES:

1957-1964 CODEN: INFI BR ISSN: 0019-9567 LANGUAGE: English PUBLISHER:  
American Society for Microbiology

8/3, K/41 (Item 21 from file: 399)

DI ALCO R File 399: CA SEARCH R

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134161879 CA: 134(12)161879u PATENT

Novel strategy for carbohydrate-based therapeutic vaccines

INVENTOR(AUTHOR): Jennings, Harold J.; Sad, Subash; Guo, Zhongnu; Liu,

Tianmin; Yang, Qining

LOCATION: Can.,

ASSIGNEE: National Research Council of Canada

PATENT: PCT International ; WO 200109298 A2 DATE: 20010208

APPLICATION: WO 2000CA886 (20000728) \*CA 2279134 (19990729)

PAGES: 25 pp. CODEN: PIXXD2 LANGUAGE: English

PATENT CLASSIFICATIONS:

CLASS: C12N 015/00A

DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ;  
CA; CH; CN; CR; CU; CZ; DE; DK; DM; DZ; EE; ES; FI; GB; GD; GE; GH; GM; HR;  
HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA;  
MD; MG; MK; MN; MW; MX; NZ; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL;  
TJ; TM; TR; TT; TZ; UA; UG; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU;  
TJ; TM DESIGNATED REGIONAL: CH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZW  
; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE;  
BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

8/3, K/42 (Item 22 from file: 399)

DI ALCOG(R) File 399: CA SEARCH(R)

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134040804 CA: 134(4)40804g JOURNAL

Biochemical engineering of surface alpha-2-8 polysialic acid for immunotargeting tumor cells

AUTHOR(S): Liu, Tianmin; Guo, Zhongwu; Yang, Qingling; Sad, Subash; Jennings, Harold J.

LOCATION: Institute for Biological Sciences, National Research Council of Canada, Ottawa, ON, Can., K1A 0R6

JOURNAL: J. Biol. Chem. DATE: 2000 VOLUME: 275 NUMBER: 42 PAGES: 32832-32836 CODEN: JBCHA3 ISSN: 0021-9258 LANGUAGE: English PUBLISHER: American Society for Biochemistry and Molecular Biology

8/3, K/43 (Item 23 from file: 399)

DI ALCOG(R) File 399: CA SEARCH(R)

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127246923 CA: 127(18)246923j JOURNAL

Differentiation and functions of T cell subsets

AUTHOR(S): Mosmann, Tim R.; Li, Li; Hengartner, Hans; Kagi, David; Fu, Wayne; Sad, Subash

LOCATION: Department of Medical Microbiology and Immunology, University of Alberta, Edmonton, Can.,

JOURNAL: Ciba Found. Symp. DATE: 1997 VOLUME: 204 NUMBER: Molecular Basis of Cellular Defence Mechanisms PAGES: 148-158 CODEN: CIBSB4 ISSN: 0300-5208 LANGUAGE: English PUBLISHER: Wiley

8/3, K/44 (Item 24 from file: 399)

DI ALCOG(R) File 399: CA SEARCH(R)

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127120355 CA: 127(9)120355g JOURNAL

Functions of CD8 T-cell subsets secreting different cytokine patterns

AUTHOR(S): Mosmann, Tim R.; Sad, Subash

LOCATION: Department of Medical Microbiology and Immunology, 632D Heritage Medical Research Centre, University of Alberta, Edmonton, AB, Can., T6H 2S2

JOURNAL: Semin. Immunol. DATE: 1997 VOLUME: 9 NUMBER: 2 PAGES: 87-92 CODEN: SEME2 ISSN: 1044-5323 LANGUAGE: English PUBLISHER: Academic

8/3, K/45 (Item 25 from file: 399)

DI ALCOG(R) File 399: CA SEARCH(R)

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127048989 CA: 127(4)48989x JOURNAL

Cytotoxicity and weak CD40 ligand expression of CD8+ type 2 cytotoxic T cells restricts their potential B cell helper activity

AUTHOR(S): Sad, Subash; Krishnan, Lakshmi; Bleackley, R. Chris; Kagi, David; Hengartner, Hans; Mosmann, Tim R.

LOCATION: Department Medical Microbiology Immunology, University Alberta, Edmonton, AB, Can.,

JOURNAL: Eur. J. Immunol. DATE: 1997 VOLUME: 27 NUMBER: 4 PAGES: 914-922 CODEN: EJIMAF ISSN: 0014-2980 LANGUAGE: English PUBLISHER: VCH

8/3, K/46 (Item 26 from file: 399)

DI ALCOG R) File 399: CA SEARCH(R)

(c) 2009 American Chemical Society. All rts. reserv.

125273312 CA: 125(21)273312z JOURNAL

Perforin and Fas killing by CD8+ T cells limit their cytokine synthesis and proliferation

AUTHOR(S): Sad, Subash; Kagi, David; Mosmann, Tim R.

LOCATION: Dep. Medical Microbiology Immunology, University Alberta, Edmonton, Can., T6G 2H7

JOURNAL: J. Exp. Med. DATE: 1996 VOLUME: 184 NUMBER: 4 PAGES: 1543-1547 CODEN: JEMEAU ISSN: 0022-1007 LANGUAGE: English

8/3, K/47 (Item 27 from file: 399)

DI ALCOG R) File 399: CA SEARCH(R)

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125139867 CA: 125(11)139867f JOURNAL

Differentiation of subsets of CD4+ and CD8+ T cells

AUTHOR(S): Mosmann, Tim R.; Sad, Subash; Krishnan, Lakshmi; Wegmann, Tom G.; Guilbert, Larry J.; Belosevic, Mke

LOCATION: Department Immunology, University Alberta, Edmonton, AB, Can., T6H 2H7

JOURNAL: Ciba Found. Symp. DATE: 1995 VOLUME: 195 NUMBER: T Cell Subsets in Infectious and Autoimmune Diseases PAGES: 42-54 CODEN: CIBSB4 ISSN: 0300-5208 LANGUAGE: English

8/3, K/48 (Item 28 from file: 399)

DI ALCOG R) File 399: CA SEARCH(R)

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124199789 CA: 124(15)199789w JOURNAL

The expanding universe of T-cell subsets: Th1, Th2 and more

AUTHOR(S): Mosmann, Tim R.; Sad, Subash

LOCATION: Dept. Medical Microbiology Immunology, Univ. Alberta, Edmonton, AB, Can., T6G 2H7

JOURNAL: Immunol. Today DATE: 1996 VOLUME: 17 NUMBER: 3 PAGES: 138-46 CODEN: IMTCDB ISSN: 0167-4919 LANGUAGE: English

8/3, K/49 (Item 29 from file: 399)

DI ALCOG R) File 399: CA SEARCH(R)

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123283376 CA: 123(21)283376w JOURNAL

Interleukin (IL) 4, in the absence of antigen stimulation, induces an energy-like state in differentiated CD8+ TCl cells: loss of IL-2 synthesis and autonomous proliferation but retention of cytotoxicity and synthesis of other cytokines

AUTHOR(S): Sad, Subash; Mosmann, Tim R.

LOCATION: Dep. Med. Microbiol. Immunol., Univ. Alberta, Edmonton, Can., T6G 2H7

JOURNAL: J. Exp. Med. DATE: 1995 VOLUME: 182 NUMBER: 5 PAGES: 1505-15 CODEN: JEMEAU ISSN: 0022-1007 LANGUAGE: English

8/3, K/50 (Item 30 from file: 399)

DI ALCOG R) File 399: CA SEARCH(R)

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122312708 CA: 122(25)312708t JOURNAL

Characterization of an immunosuppressive factor secreted by a human

10563731a.txt  
trophoblast-derived choriocarcinoma cell line  
AUTHOR(S): Krishnan, Lakshmi; Sad, Subash; Raghupathy, Raj  
LOCATION: Immunogenetics Lab., National Inst. Immunol., New Delhi, 110067  
India  
JOURNAL: Cell. Immunol. DATE: 1995 VOLUME: 162 NUMBER: 2 PAGES:  
295-308 CODEN: CLIMB8 ISSN: 0008-8749 LANGUAGE: English

8/3, K/51 (Item 31 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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122237713 CA: 122(19)237713k JOURNAL  
Cytokine-induced differentiation of precursor mouse CD8+ T cells into  
cytotoxic CD8+ T cells secreting Th1 or Th2 cytokines  
AUTHOR(S): Sad, Subash; Marcotte, Rita; Mbsmann, Tim R  
LOCATION: Department Immunology, University of Alberta, Edmonton, AB,  
Can.

JOURNAL: Immunity DATE: 1995 VOLUME: 2 NUMBER: 3 PAGES: 271-9  
CODEN: IUNIEH ISSN: 1074-7613 LANGUAGE: English

8/3, K/52 (Item 32 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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120104362 CA: 120(9)104362g JOURNAL  
Synthetic gonadotropin-releasing hormone (GnRH) vaccines incorporating  
GnRH and synthetic T-helper epitopes  
AUTHOR(S): Sad, Subash; Chauhan, V.S.; Arunan, K; Raghupathy, Raj  
LOCATION: Nat. Inst. Immunol., New Delhi, India  
JOURNAL: Vaccine DATE: 1993 VOLUME: 11 NUMBER: 11 PAGES: 1145-50  
CODEN: VACCDE ISSN: 0264-410X LANGUAGE: English

8/3, K/53 (Item 33 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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115110360 CA: 115(11)110360t JOURNAL  
Organization and chromosomal localization of .beta.-tubulin genes in  
Leishmania donovani  
AUTHOR(S): Sad, Saumitra; Adhya, Sanit  
LOCATION: Leishmania Group, Indian Inst. Chem Biol., Calcutta, 700 032,  
India

JOURNAL: J. Biosci. DATE: 1990 VOLUME: 15 NUMBER: 4 PAGES: 239-48  
CODEN: JCBSDN ISSN: 0250-5991 LANGUAGE: English

8/3, K/54 (Item 34 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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115106492 CA: 115(11)106492v JOURNAL  
Influence of the genetic background and carrier protein on the antibody  
response to GnRH  
AUTHOR(S): Sad, Subash; Talwar, G. P.; Raghupathy, Raj  
LOCATION: Natl. Inst. Immunol., New Delhi, 110067, India  
JOURNAL: J. Reprod. Immunol. DATE: 1991 VOLUME: 19 NUMBER: 2 PAGES:  
197-207 CODEN: JRIHDR ISSN: 0165-0378 LANGUAGE: English  
? s (lip? or liposom?) and (polar or fraction or chromatag? or extract? or separat?  
or solub?)  
Processing

Processed 10 of 56 files ...  
 Processing  
 Processed 20 of 56 files ...  
 Processing  
 Processed 30 of 56 files ...  
 Completed processing all files  
 6244416 LI P?  
 366990 LI POSOMP?  
 766560 POLAR  
 2532715 FRACTION  
 171 CHROMATAG?  
 5783831 EXTRACT?  
 6883589 SEPARAT?  
 2720157 SOLUB?  
 S9 864532 (LI P? OR LI POSOMP?) AND (POLAR OR FRACTION OR CHROMATAG?  
 OR EXTRACT? OR SEPARAT? OR SOLUB?)  
 ? s s9 and (Mycobac? or (bcg or bovis))  
 864532 S9  
 645888 MYCOBAC?  
 147327 BCG  
 103950 BOVIS  
 S10 8125 S9 AND (MYCOBAC? OR (BCG OR BOVIS))  
 ? s s10 and (mannoside or manno?)  
 8125 S10  
 10056 MANNOSIDE  
 312247 MANNO?  
 S11 665 S10 AND (MANNOSIDE OR MANNO?)  
 ? s s11 and (chloroform)  
 665 S11  
 229026 CHLOROFORM  
 S12 36 S11 AND (CHLOROFORM)  
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>>>Duplicate detection is not supported for File 393.

>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.

S13 14 RD (unique items)

? t s13/3, k/1-14

>>>KWC option is not available in file(s): 399

13/3, K/1 (Item 1 from file: 5)

DI ALCOG R) File 5: Biosis Previews(R)

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18055063 BIOSIS NO.: 200400425852

Activation of dendritic cells by liposomes prepared from

phosphatidylinositol mannosides from Mycobacterium

bovis bacillus Calmette-Guerin and adjuvant activity in vivo

AUTHOR: Sprott G Dennis (Reprint); Dicaire Chantal J; Gurnani Kornal; Sad

Subash; Krishnan Lakshmi

AUTHOR ADDRESS: Inst Biol Sci, Natl Res Council Canada, 100 Sussex Dr,

Ottawa, ON, K1A 0P6, Canada\*\*Canada

AUTHOR E-MAIL ADDRESS: dennis.sprott@nrc-cnrc.gc.ca

JOURNAL: Infection and Immunity 72 (9): p5235-5246 September 2004 2004

MEDIUM: print

ISSN: 0019-9567 (ISSN print)

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

Activation of dendritic cells by liposomes prepared from

10563731a.txt

phosphatidylinositol mannosides from *Mycobacterium bovis* bacillus Calmette-Guérin and adjuvant activity in vivo

**ABSTRACT:** Liposome vesicles could be formed at 65degreeC from the chloroform soluble, total polar lipids (TPL) extracted from *Mycobacterium bovis* bacillus Calmette-Guérin (BCG). Mice immunized with ovalbumin (OVA) entrapped in TPL liposomes produced both anti-OVA antibody and cytotoxic T lymphocyte responses. Murine bone marrow-derived dendritic...

...6 (IL-6), IL-12, and tumor necrosis factor upon exposure to antigen-free TPL liposomes. Three phosphoglycerolipids and three phospholipids comprising 96% of TPL were identified as phosphatidylinositol dimannoside, palmitoyl-phosphatidylinositol dimannoside, di palmitoyl-phosphatidylinositol dimannoside, phosphatidylinositol, phosphatidylethanolamine, and cardiolipin. The activation of dendritic cells by liposomes prepared from each purified lipid component of TPL was evaluated in vitro. A basal activity of phosphatidylinositol liposomes to activate proinflammatory cytokine production appeared to be attributable to the tuberculosteric fatty acyl 19:0 chain characteristic of mycobacterial glycerolipids, as similar lipids lacking tuberculosteric chains showed little activity. Phosphatidylinositol dimannoside was identified as the primary lipid that activated dendritic cells to produce amounts of proinflammatory cytokines several times higher than the basal level, indicating the importance of mannose residues. Although the activity of phosphatidylinositol dimannoside was little influenced by palmitoylation of mannose at C-6, a further palmitoylation at inositol C-3 diminished the induction levels of IL-6 and IL-12. Further, OVA entrapped in palmitoyl-phosphatidylinositol dimannoside liposomes was delivered to dendritic cells for major histocompatibility complex class I presentation more effectively than TPL OVA-liposomes. BCG liposomes containing mannose lipids caused up-regulation of costimulatory molecules and CD40. Thus, the inclusion of pure phosphatidylinositol mannosides of BCG in lipid vesicle vaccines represents a simple and efficient option for targeting antigen delivery and providing immune...

**DESCRIPTION:**

...BIOSYSTEMATIC NAMES: *Mycobacteriaceae*----

...*Mycobacteria*, *Actinomycetes* and *Related Organisms*, *Eubacteria*,  
*Bacteria*, *Microorganisms*  
...ORGANISMS: BCG (*Mycobacteriaceae*); ...

...*Mycobacterium bovis* (*Mycobacteriaceae*)  
CHEMICALS & BIOCHEMICALS: ...liposomes-----

...phosphatidylinositol mannosides--

BIOSYSTEMATIC CODES:

...08881 *Mycobacteriaceae*

COMMON TAXONOMIC TERMS:

13/3, K/2 (Item 2 from file: 5)  
DIALOG(R) File 5: Biosis Previews(R)  
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17113636 BIOSIS NO.: 200300072355  
Identification of the bound and unbound lipids on the cell envelopes of *Mycobacterium bovis*.

AUTHOR: Dandapat P (Reprint); Verma Rishendra; Venkatesan K (Reprint);  
Sharma V D (Reprint); Katoch V M (Reprint)

10563731a.txt

AUTHOR ADDRESS: Central JALMA Institute for Leprosy, Agra, UP, 280 205,  
India\*\*India  
JOURNAL: Indian Journal of Animal Sciences 72 (11): p946-950 November 2002  
2002  
MEDLINE print  
ISSN: 0367-8318 (ISSN print)  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

Identification of the bound and unbound lipids on the cell envelopes  
of *Mycobacterium bovis*.

ABSTRACT: Sixteen *Mycobacterium bovis* isolates from bovine  
tissues and one reference strain M. bovis AN5 were investigated for  
different bound and unbound lipids. For comparison, other  
mycobacterial species included in the study were M. tuberculosis,  
M. bovis BCG and M. avium. The thin layer chromatographic  
(TLC) study indicated the absence of C-mycosides in all the M.  
bovis isolates while phosphatidyl inositol mannosides (PIMs)  
was present in all M. bovis isolates, M. bovis BCG and  
M. tuberculosis as shown by TLC with the solvent chloroform  
-methanol-water (60:30:6, v/vX1). The polar glycolipids were  
present in all the M. bovis isolates and M. tuberculosis showing  
seven bands with R<sub>f</sub> value 0.62, 0.55, 0...

...0.89) (75:22:3, v/vX1). The unidimensional TLC mycolates patterns of all  
M. bovis isolates including AN5 showed one spot corresponding to  
alpha-mycolate (as in M. tuberculosis) and...

#### DESCRIPTORS:

BIOSYSTEMATIC NAMES: Mycobacteriaceae-...

...Mycobacteria, Actinomycetes and Related Organisms, Eubacteria,  
Bacteria, Microorganisms

ORGANISMS: *Mycobacterium bovis* (Mycobacteriaceae)-...

...pathogen, strain-BCG strain-AN5...

...*Mycobacterium tuberculosis* (Mycobacteriaceae)-...

...*Mycobacterium avium* (Mycobacteriaceae)-

DISEASES: *Mycobacterium bovis* infection...

MESH TERMS: *Mycobacterium* Infections (MeSH)

CHEMICALS & BIOCHEMICALS: Lipids-...

...phosphatidyl inositol mannosides

#### BIOSYSTEMATIC CODES:

08881 Mycobacteriaceae

#### COMMON TAXONOMIC TERMS:

13/3, K/3 (Item 3 from file: 5)  
DIALOG(R) File 5: Biosis Previews(R)  
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15159368 BIOSIS NO.: 199900419028

Production and partial characterization of antibody to cord factor  
(trehalose 6,6'-dimycolate) in mice

AUTHOR: Fujiwara Nagatoshi; Oka Shiro; Ide Michio; Kashima Kazutoshi; Honda  
Takeshi; Yano Ikuya (Reprint)

AUTHOR ADDRESS: Department of Bacteriology, Osaka City University Medical

10563731a.txt

School, 1-4-3 Asahi-machi, Abeno-ku, Osaka, Osaka, 545-8585, Japan\*\*Japan  
JOURNAL: Microbiology and Immunology 43 (8): p785-793 1999 1999

MEDI UM: print

ISSN: 0385-5600

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

...ABSTRACT: water micelles without carrier protein. The antigenic TDM was isolated and purified chromatographically from the chloroform-methanol extractable lipids of R. ruber. The hydrophobic moiety of this TDM was composed of two molecules of...

...glycosyl monomycolates differing in the carbohydrate moiety, such as that of glucose mycolate (GM) and mannose mycolate (MM), obtained from R. ruber. Moreover, the antibody reacted against mycolic acid methyl ester itself...

...mouse myeloma cells to examine its biological activities and the role of humoral immunity in mycobacterial infection. MoAb reacted against the TDM glycosyl mycolate, and mycolic acid methyl ester in ELISA...

13/3, K/4 (Item 4 from file: 5)

DI ALCO (R) File 5: Biosis Previews(R)

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08714564 BIOSIS NO.: 198784068713

LIPOLYSACCHARIDE ISOLATED FROM MYCOBACTERIUM TUBERCULOSIS

STRAIN AOYAMA B

AUTHOR: KOBATAKE H (Reprint); KUMAGAI K; KITAGAWA O; NIWA S-I

AUTHOR ADDRESS: CENTRAL RES. LAB., ZERIA PHARMACEUTICAL CO. LTD., OSHIKIRI

2512, KONAN-MACHI, SAITAMA 360-01, JPN\*\*JAPAN

JOURNAL: Agricultural and Biological Chemistry 51 (3): p691-698 1987

ISSN: 0002-1369

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

LIPOLYSACCHARIDE ISOLATED FROM MYCOBACTERIUM TUBERCULOSIS

STRAIN AOYAMA B

ABSTRACT: Methods for efficient extraction and simple purification of the lipopolysaccharide specific for Mycobacterium tuberculosis were developed. Crude lipopolysaccharide was obtained from sterilized cells through mechanical disintegration, Triton X-100 extraction, ethanol precipitation, glucosidase digestion, and gel-filtration chromatography. The lipopolysaccharide was further purified by treatments with pyridine-methanol and chloroform-methanol to remove the contaminating glycolipids and phospholipids, and by digestion with the immobilized trypsin to remove the contaminating proteins. The purified lipopolysaccharide was composed of a polysaccharide consisting of D-mannose and D-arabinose, and fatty acids, mainly palmitic, tuberculoheptanoic, and stearic acids, which were bound in ester linkages. The lipopolysaccharide had strong tumor regressing activity on the mouse fibrosarcoma.

DESCRIPTORS:

BIOSYSTEMATIC NAMES: Mycobacteriaceae-...

...Mycobacteria, Actinomycetes and Related Organisms, Eubacteria,

Bacteria, Microorganisms

CHEMICALS & BIOCHEMICALS:

BIO SYSTEMATIC CODES:  
08881 Mycobacteriaceae

COMMON TAXONOMY TERMS:

13/3, K/5 (Item 1 from file: 155)  
DIALOG R File 155: MEDLINE (R)  
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04722358 PMID: 4808895 Record Identifier: PMC246531  
Biosynthesis of glycosyl diglycerides in *Mycobacterium smegmatis*.  
Schultz J C; Elbein A D  
Journal of bacteriology (UNITED STATES) Jan 1974, 117 (1) p107-15,  
ISSN 0021-9193--Print Journal Code: 2985120R  
Publishing Model Print  
Document type: Journal Article  
Languages: ENGLISH  
Main Citation Owner: NLM  
Other Citation Owner: NLM  
Record type: MEDLINE; Completed

Biosynthesis of glycosyl diglycerides in *Mycobacterium smegmatis*.  
A particulate enzyme preparation from *Mycobacterium smegmatis* catalyzes the transfer of [(14)C]galactose from uridine 5'-diphosphate (UDP)-[(14)C]galactose and of [(14)C]glucose from UDP-[(14)C]glucose into chloroform-soluble products. The radioactive neutral lipids were purified by passage through diethylaminoethyl-cellulose, followed by thin-layer chromatography. When UDP-glucose was used as substrate, two major radioactive lipids were obtained; one had a hexose-glucose-glycerol ratio of 1:1:1. The second...  
... hexose-glycerol ratio of 2:1 and, in addition to glucose, contained lesser amounts of mannose and galactose. With UDP-galactose as substrate, two radioactive products were observed that were chromatographically...

... labeled mono- and diglycosyl diglyceride. Palmitate and oleate were the predominant fatty acid constituents in these lipids and were present in equimolar amounts in all of the products examined. The products have...

... been identified as monoglycosyl diglyceride and a diglycosyl diglyceride containing glucose as the major hexose along with mannose and galactose. Properties of the galactosyl and glucosyl transferases are described.

Descriptors: \*Glycerides--biosynthesis--BI; \*Lipids--biosynthesis--BI; \*Mycobacterium--metabolism--ME...; metabolism--ME; Glucosylases--metabolism--ME; Glycerides--analysis--AN; Glycerol phosphate Dehydrogenase--analysis--AN; Hydrogen-Ion Concentration; Lipids--analysis--AN; Mannose--analysis--AN; Mycobacterium--analysis--AN; Nucleoside Diphosphate Sugars--metabolism--ME; Oleic Acids--analysis--AN; Palmitic Acids--analysis--AN...

Chemical Name: Carbon Radioisotopes; Glycerides; Lipids; Nucleoside Diphosphate Sugars; Oleic Acids; Palmitic Acids; Galactose; Mannose; Glucose; Uridine; Glycerol phosphate Dehydrogenase; Galactosylases; Glucosylases

13/3, K/6 (Item 2 from file: 155)  
DIALOG R File 155: MEDLINE (R)  
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04208701 PMID: 5001480  
A comparison of the chemical composition of *Mycobacterium*  
Page 50

tuberculosis muris with Mycobacterium tuberculosis bovis (

BOG)

Caldes G, Prescott B  
 Biochemical and biophysical research communications (UNITED STATES) Aug  
 20 1971, 44 (4) p852-8, ISSN 0006-291X-Print Journal Code: 0372516  
 Publishing Model Print  
 Document type: Journal Article  
 Languages: ENGLISH  
 Main Citation Owner: NLM  
 Record type: MEDLINE; Completed

A comparison of the chemical composition of Mycobacterium  
 tuberculosis muris with Mycobacterium tuberculosis bovis (

BOG)

Descriptors: \*Mycobacterium bovis--analysis--AN; \*  
 Mycobacterium tuberculosis--analysis--AN; Amino Acids--analysis--AN;  
 Arabinose--analysis--AN; Chloroform Chromatography, Ion Exchange;  
 Chromatography, Paper; Ethanol; Ethyl Ethers; Galactose--analysis--AN;  
 Glucose--analysis--AN; Hexosamines--analysis--AN; Lipids--analysis--AN;  
 Mannose--analysis--AN; Ribose--analysis--AN; Solubility;  
 Species Specificity

Chemical Name: Amino Acids; Ethyl Ethers; Hexosamines; Lipids;  
 Arabinose; Galactose; Mannose; Ribose; Glucose; Ethanol;  
 Chloroform

13/3, K/7 (Item 1 from file: 370)

DIALOG File 370: Science

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00508546 (USE 9 FOR FULLTEXT)

CD1d-Restricted Immunoglobulin G Formation to GPI-Anchored Antigens

Mediated by NKT Cells

Schofield, Louis; McConville, Malcolm J.; Hansen, Diana; Campbell, A.  
 Stewart; Fraser-Reid, Bert; Grusby, Michael J.; Tachado, Souvenir D.  
 L. Schofield, D. Hansen, S. D. Tachado, Walter and Eliza Hall Institute of  
 Medical Research, Post Office, Royal Melbourne Hospital, Victoria 3050,  
 Australia. M. J. McConville, Department of Biochemistry and Molecular  
 Biology, University of Melbourne, Victoria 3052, Australia. A. Stewart  
 Campbell, INSMED Pharmaceuticals, 880 East Leigh Street, Richmond, VA  
 23219, USA. B. Fraser-Reid, Natural Products and Glycotechnology, 4118  
 Swarthmore Road, Durham NC 27707, USA. M. J. Grusby, Department of  
 Immunology and Infectious Diseases, Harvard School of Public Health, and  
 Department of Medicine, Harvard Medical School, Boston, MA 02115, USA.

Science Vol. 283 5399 pp. 225

Publication Date: 1-08-1999 (990108) Publication Year: 1999

Document Type: Journal ISSN: 0036-8075

Language: English

Section Heading: Reports

Word Count: 2490

(THIS IS THE FULLTEXT)

...Text: related human CD1b and CD1c molecules can elicit cytolytic and  
 interferon- (gamma) responses by presenting mycobacterial glycolipid  
 antigens to CD8.sup(+) or CD4.sup(-) CD8.sup(-) T cells (B4). Murine V...

...be GPIs (B6). Therefore, CD4.sup(+) NKT cells may participate in  
 CD1d-restricted recognition of lipid antigens. However, the natural  
 ligand and functional significance of NKT cells in immune responses in...

...molecule was confirmed by gas chromatography-mass spectrometry (GC-MS).  
 In addition, a phosphorylated and lipidated mammalian GPI based on  
 the rat brain Thy-1 GPI (Fig. 1C), and the corresponding

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inositol phosphoglycan (IPG) lacking a lipid tail, both chemically synthesized by n-pentenyl glucoside strategy and compositionally pure by .sup(1)...

...in class II.sup(-/-) mice with the mfVSG of T. brucei, but not the deacylated soluble VSG derived by PI-specific phospholipase C (PI-PLC) hydrolysis (Fig. 1A), demonstrating that the GPI lipid domain is required, and the GPI glycan is not sufficient, for the phenomenon. This was...

...responses in class II.sup(-/-) mice require linkage of antigen to GPI with an intact lipid, which may be composed of diacylglycerol or alkylacylglycerol...IM GPIs of L. mexicana. Nomenclature is as described (B14), where all isomers contain one mannose in a1-3 linkage, EP indicates ethanolamine phosphate, and M2 and M4 indicate the number of mannose residues, as shown. (Q) Chemically synthesized rat brain Thy-1 GPI...

#### References and Notes:

...anchored P. falciparum proteins, purified by high-performance liquid chromatography and affinity chromatography (27), were extracted in chloroform/methanol (2:1), precipitated with acetone, solubilized and reduced, diluted in 5 mM CaCl<sub>2</sub> inf(2), digested for 72 hours at 37...

...and purified by high-performance thin-layer chromatography (HPTLC) (R<sub>inf</sub> = 0.05) with chloroform/methanol/acetic acid/water (C/M/HaC/W 25:15:4:2), QMW(1:2:0.8) extracts of L. mexicana promastigotes were purified over Octyl-Sepharose followed by HPTLC with a solution...

13/3/K/8 (Item 2 from file: 370)

DIALOG(R) File 370: Science

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00503975 (USE 9 FOR FULLTEXT)

Structural Requirements for Glycolipid Antigen Recognition by CD1b-Restricted T Cells

Moody, D. Branch; Reinhold, Bruce B.; Guy, Mark R.; Beckman, Evan M.; Frederique, Daphney E.; Furlong, Stephen T.; Ye, Song; Reinhold, Vernon N.; Sieling, Peter A.; Modlin, Robert L.; Besra, Gurdayal S.; Porcelli, Steven A.

D. B. Moody, E. M. Beckman, D. E. Frederique, S. T. Furlong, S. A. Porcelli, Lymphocyte Biology Section, Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02115, USA.; B. B. Reinhold, S. Ye, V. N. Reinhold, Mass Spectrometry Unit, Boston University School of Medicine, Boston, MA 02118-2394, USA.; M. R. Guy and G. S. Besra, Department of Microbiology, Colorado State University, Fort Collins, CO 80523-1677, USA.; P. A. Sieling and R. L. Modlin, Division of Dermatology and Department of Microbiology and Immunology, UCLA School of Medicine, Los Angeles, CA 90033, USA.

Science Vol. 278 5336 pp. 283

Publication Date: 10-10-1997 (971010) Publication Year: 1997

Document Type: Journal ISSN: 0036-8075

Language: English

Section Heading: Reports

Word Count: 2372

(THIS IS THE FULLTEXT)

Abstract: The human CD1b protein presents lipid antigens to T cells, but the molecular mechanisms is unknown. Identification of mycobacterial glucose monomycolate (GMM) as a CD1b-presented

glycolipid allowed determination of the structural requirements for...

...of GMM to CD1b-restricted T cells was not affected by substantial variations in its lipid tails, but was extremely sensitive to chemical alterations in its carbohydrate or other polar substituents. These findings support the view that the recently demonstrated hydrophobic CD1 groove binds the acyl chains of lipid antigens relatively nonspecifically, thereby positioning the hydrophilic components for highly specific interactions with T cell...

...Text: At least two human CD1 proteins (CD1b and CD1c) mediate specific T cell recognition of bacterial lipid and glycolipid antigens (B3) (B4) (B5) (B6). Two classes of CD1-restricted lipid antigens-mycolic acids and phosphoglycolipids such as phosphatidylinositol mannosides (PIMs) or lipoarabinomannan (LAM) (B4) (B5) -have been identified. To find other antigens presented by the CD1 system, we established additional T cell lines specific for mycobacterial lipid antigens. Analysis of the CD4.sup(-)CD8.sup(-) TCR $\alpha$  (beta).sup(+) T cell line LDN5, isolated from a skin biopsy of a cutaneous reaction to Mycobacterium leprae antigen, revealed evidence for a third class of CD1-restricted lipid antigens (B7...

...LDN5 proliferated to only one lipid fraction separated by preparative thin-layer chromatography (TLC) from organic extracts of M. leprae and cross-reacted strongly with a lipid of identical retardation factor (R<sub>inf</sub>(f)) extracted from M. phlei (B8). TLC staining indicated that the lipid contained carbohydrate (anthrone positive) but not phosphate (molybdenum negative), distinguishing this antigen from the two...

...The structures of the lipid and carbohydrate moieties of the antigenic glycolipid were determined separately. The products resulting from alkaline hydrolysis of the antigen were partitioned and recovered separately from organic and aqueous phases. The organic phase lipids coeluted on high-pressure liquid chromatography (HPLC) with mycobacterial mycolic acids (B4), and the aqueous phase contained a single product that was identified as...

...This composition analysis suggested that the glycolipid antigen was glucose monomycolate (GMM), a previously described mycobacterial cell wall component consisting of a single glucopyranoside residue esterified at its sixth carbon to...

...containing a monounsaturated, C<sub>inf</sub>(80) wax-ester mycolic acid (Fig. 1C) (B10). GMM was separately isolated from trehalose dimycolate (cord factor) treated with aqueous acid, which released intact GMM by...

...We determined the role of the lipid portion of GMM in T cell recognition by isolating GMM from mycobacterial species that differ in mycolic acid composition. Mycobacterium bovis BCG, M. fortuitum, M. smegmatis, and M. phlei produce GMMs consisting of glucose esterified to mycolic...

...B11). This antigen lacked long chain length (compared with C<sub>inf</sub>(80) mycolic acids of mycobacteria), cyclopropanation, double bonds, and R groups, ruling out all of these natural chemical variations of...

...LDN5, we considered whether the spectrum of antigenic glycolipids might be extremely broad (any glucosylated lipid) or be limited to mycolyl glycolipids. Mycolyl glycolipids are defined by the ...ators (B14). Therefore, recognition of GMM was absolutely dependent on the  $\alpha$ -branched, (beta)-hydroxy lipid structure that defines mycolyl lipids, but the long distally substituted acyl chains found in many naturally occurring mycolic acids were...

...The role of the carbohydrate moiety of the glycolipid in T cell recognition was separately evaluated. The CD1b-restricted response of LDN5 to GMM was carbohydrate dependent, because free mycolic...

...cell response to mycolyl glycolipids most similar to GMM we prepared two stereoisomers of GMM, mannose monomycolate and galactose monomycolate (B13). LDN5 proliferated at similar doses to natural and semisynthetic GMM. In contrast, LDN5 responded very weakly or not at all to mannose monomycolate and galactose monomycolate, epimers of GMM at the 2 or 4 positions of the...

...The identification of this third class of lipid antigens revealed a general motif for CD1b-restricted lipid antigens. Synthetic GMMs intermediate in structure between the two previously known antigens, P1M and...

...mycolic acid, but like P1M is glycosylated. The long (C18(80)) and distally substituted lipid moiety of natural GMM was shortened (C18(32)) and simplified (Fig. 2C) to take...

...the two saturated acyl chains of P1M without losing antigenicity, as long as the branched lipid structure was maintained (Fig. 2D). Thus, CD1b-restricted antigens from each of the three classes...

...The identification of this motif should guide the search for new foreign and potentially self lipid antigens. For example, these results demonstrate that glycolipids with short-chain mycolic acids characteristic of...

...to the exterior of the protein through a narrow opening lined by conserved charged and polar amino acids above the F (prime) pocket (B16). Thus, in terms of size, shape, and electrostatic topography, the CD1 ligand-binding groove is ideally suited to interact with lipids conforming to the CD1b antigen motif with the two acyl chains buried within the A...

...F (prime) pockets. This mechanism of binding would leave the hydrophilic cap to interact with polar and charged amino acids at the entrance to the groove (Fig. 4) (B17). In the straightforward structural model provides a mechanism by which T cells specifically interact with unconstrained, hydrophobic lipid antigens in an aqueous environment. Detailed structural studies of this model will reveal how the...

...tetanus toxoid-specific (tet tox); 10 (mu) g/ml] and DN6 [CD1c-restricted, M tuberculosis lipid-specific (Tb organic); 1/200 dilution], two examples shown here. Stimulation index was calculated as...

...Figure Removed

#### Figure F2

Caption: The fine structure of the lipid moiety of GMM did not determine T cell recognition. (A) LDN5 proliferated in response to GMM from all strains tested [M phlei ((square-solid)), BOG (square), M smegmatis (triangle), and M fortuitum (down triangle, filled)] but not to trehalose dimycolate...

...of 1:1 corresponded to the concentration of GMM recovered from preparative TLC of organic extract from 15 mg of each bacterium (B8). (B) LDN5 lysed C1R lymphoblastoid target cells (effector)...

...to natural or semisynthetic GMM at similar doses, but gave only a trace response to mannose monomycolate and no response to galactose monomycolate. These mannose- and galactose-containing mycolyl lipids differ from GMM only in the orientation of a single hydroxyl

group at the 2...

... Figure F4

Caption: Structural motif for CD1b-restricted antigens. Each of the known CD1b-restricted lipid antigens contains a proximally branched acyl chain or two acyl chains capped by a hydrophilic...

#### References and Notes:

- ...8. *Mycobacterium phlei*, *M. tuberculosis* H37Ra, *M. fortuitum* M smegmatis, and *M. bovis* BCG were cultivated in 7H9 medium (Difco) supplemented with 0.05% Tween-80 and 1% glucose, mannose, or galactose. Organic extracts (1 x) were made by shaking 7.5 mg of lyophilized bacteria per 1 ml of chloroform:methanol (2:1) at 20 Deg. C for 2 hours. Sonicates (1 x) were made...B6). Mycolyl glycolipids were purified with preparative silica TLC in solvent A (60:16:2 chloroform:methanol:water) and extraction from silica into chloroform:methanol (2:1) or by eluting an open 2 cm by 20 cm silica column serially with chloroform and acetone in a stepwise gradient. The antigenic glycolipid eluted in 30% acetone in chloroform ;
- ... glycolipid was hydrolyzed, and the resulting products were partitioned between aqueous and organic phases. Organic soluble products were derivatized with phenacyl bromide and coeluted on C18 reversed-phase HPLC with M...
- ...on a Quattro II triple quadrupole mass spectrometer in the positive mode with samples in chloroform:methanol (2:1) at a flow rate of 2 to 4 (mu) l/min...
- ...12. *Mycobacterium bovis* BCG and *M. tuberculosis* mycolic acids contain cyclopropyl groups, whereas *M. smegmatis* mycolic acids contain double...
- ...and a (prime) mycolates) or named R groups as follows: *M. tuberculosis* (a, keto, methoxy); BCG (a, keto); *M. phlei* (a, wax-ester, and possibly small amounts of keto); and M...
- ...A. Nashed, L. Anderson, Carbohydr. Res. 218, 95 (1991)] were used, except that the appropriate lipid [3-hydroxypalmitate (Matreya), tetradecylhexadecanoate (Vako), or triacontanoate (Sigma)] or carbohydrate [glucose, mannose, or galactose (Sigma)] were substituted in the reactions. "Natural" hexose mycolates were isolated from *M. phlei* grown in glucose-, galactose-, or mannose-supplemented media [Y. Natsuhara, S. Oka, K. Kaneda, Y. Kato I. Yano, Cancer Immunol. Immunother...
- ...G. S. Besra et al., Proc. Natl. Acad. Sci. U.S.A. 91, 12735 (1994). Lipid structures were confirmed by ESI-MS and TLC. Nuclear magnetic resonance analysis of semisynthetic hexose...processing, as was the case for CD1b-restricted recognition of mycolic acid (B3) (B4) and lipoglycans (B5). Treatment of macrophages with 25 mM chloroquine reduced the proliferative response of LDN5 to...
- ...17. The CD1-lipid antigen association is predicted to occur with an orientation similar to that of phosphatidylcholine in...

Beilstein Abstract Id: 5885241

Title: Lipopolysaccharide Isolated from Mycobacterium tuberculosis Strain Aoyama B  
 Document Type: Journal Record Type: Abstract  
 Author: Kobatake, Hiroshi; Kuragai, Kazuhiro; Kitagawa, Osamu; Niwa, Sei-ichi  
 Citation: Agric. Biol. Chem. (1987) Series: 51-3, 691-698 CODEN: ABCHA6  
 Language: English  
 Abstract Language: English

Title: Lipopolysaccharide Isolated from Mycobacterium tuberculosis Strain Aoyama B  
 Abstract: Methods for efficient extraction and simple purification of the lipopolysaccharide specific for Mycobacterium tuberculosis were developed. Crude lipopolysaccharide was obtained from sterilized cells through mechanical disintegration, Triton X-100 extraction, ethanol precipitation, glucosidase digestion, and gel-filtration chromatography. The lipopolysaccharide was further purified by treatments with pyridine-methanol and chloroform-methanol to remove the contaminating glycolipids and phospholipids, and by digestion with the immobilized trypsin to remove the contaminating proteins. The purified lipopolysaccharide was composed of a polysaccharide consisting of D-mannose and D-arabinose, and fatty acids, mainly palmitic, tuberculostearic, and stearic acids, which were bound in ester linkages. The lipopolysaccharide had strong tumor regressing activity on the mouse fibrosarcoma.

13/3, K/10 (Item 1 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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138152262 CA: 138(11)152262 PATENT  
 Vaccine adjuvant properties of liposomes formed at elevated temperatures from the polar chloroform extractable lipids from Mycobacterium bovis BCG  
 INVENTOR(AUTHOR): Sprott, G Dennis; Krishnan, Lakshmi; Sad, Subash  
 LOCATION: Can.,  
 ASSIGNEE: National Research Council of Canada  
 PATENT: PCT International ; WO 200311336 A2 DATE: 20030213  
 APPLICATION: WO 2002CA1217 (20020802) \* US PV309512 (20010803)  
 PAGES: 46 pp. CODEN: PIXD2 LANGUAGE: English  
 PATENT CLASSIFICATIONS:

CLASS: A61K-039/39A; A61K-009/127B; A61P-037/04B; A61P-035/00B

DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VN; YU; ZA; ZM; ZW  
 AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZM; ZW AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; SK; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG

13/3, K/11 (Item 1 from file: 135)

DIALOG(R) File 135: NewsRx Weekly Reports

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0000171563 (USE FORMAT 7 OR 9 FOR FULLTEXT)

Liposomes prepared from BCG possessed adjuvant activity in vivo

Immunotherapy Weekly, November 10, 2004, p.224

DOCUMENT TYPE: Expanded Reporting LANGUAGE: English  
 RECORD TYPE: FULLTEXT  
 WORD COUNT: 481

Liposomes prepared from BCG possessed adjuvant activity in vivo

TEXT: Liposomes prepared from phosphatidylinositol mannosides from *Mycobacterium bovis* bacillus Calmette-Guerin (BCG) activated dendritic cells and possessed adjuvant activity in vivo.

According to a study from Canada, "Liposome vesicles could be formed at 65 degrees C from the chloroform soluble, total polar lipids (TPL) extracted from *Mycobacterium bovis* bacillus Calmette-Guerin (BCG). Mice immunized with ovalbumin (OVA) entrapped in TPL liposomes produced both anti-OVA antibody and cytotoxic T lymphocyte responses. Murine bone marrow-derived dendritic...  
 ...6 (IL-6), IL-12, and tumor necrosis factor upon exposure to antigen-free TPL liposomes."

... and colleagues at the National Research Council of Canada. "The activation of dendritic cells by liposomes prepared from each purified lipid component of TPL was evaluated in vitro."

"A basal activity of phosphatidylinositol liposomes to activate proinflammatory cytokine production appeared to be attributable to the tuberculosteric fatty acyl 19:0 chain characteristic of mycobacterial glycerolipids, as similar lipids lacking tuberculosteric chains showed little activity," reported the researchers. "Phosphatidylinositol di-mannoside was identified as the primary lipid that activated dendritic cells to produce amounts of proinflammatory cytokines several times higher than the basal level, indicating the importance of mannose residues."

"Although the activity of phosphatidylinositol di-mannoside was little influenced by palmitoylation of mannose at C-6, a further palmitoylation at inositol C-3 diminished the induction levels of...

...and IL-12," stated Sprott and his collaborators. "Further, OVA entrapped in palmitoyl-phosphatidylinositol di-mannoside liposomes was delivered to dendritic cells for major histocompatibility complex class I presentation more effectively than TPL OVA-liposomes. BCG liposomes containing mannose lipids caused up-regulation of costimulatory molecules and CD40."

"Thus, the inclusion of pure phosphatidylinositol mannosides of BCG in lipid vesicle vaccines represents a simple and efficient option for targeting antigen delivery and providing immune...

...published the results of their research in *Infection and Immunity* (Activation of dendritic cells by liposomes prepared from phosphatidylinositol mannosides from *Mycobacterium bovis* bacillus Calmette-Guerin and adjuvant activity in vivo. *Infect Immun*, 2004; 72(9): 5235-5246...

... USA

The information in this article comes under the major subject areas of Vaccine Adjuvant, Mycobacteria, Vaccine Development, Liposomes, Vaccine Delivery, Immunology, and Immunotherapy.

This article was prepared by Immunotherapy Weekly editors from staff

...

0309681 DBR Accession No.: 2003-11466 PATENT  
 Novel liposome useful for activating dendritic cells or as  
 immunomodulating carriers for antigens in vaccines, comprises a  
 chloroform soluble and extractable total polar  
 lipid of *Mycobacterium* species - *Mycobacterium*  
*bovis* or BCG lipid, chloroform soluble  
 liposome characterization useful for cancer and infection therapy  
 AUTHOR: SPROTT G D; KRI SHAN L; SAD S  
 PATENT ASSIGNEE: NAT RES COUNCIL CANADA 2003  
 PATENT NUMBER: WO 2003011336 PATENT DATE: 20030213 WPI ACCESSION NO.:  
 2003-239475 (200323)  
 PRIORITY APPLC NO.: US 309512 APPLC DATE: 20010803  
 NATIONAL APPLC NO.: WO 2002CA1217 APPLC DATE: 20020802  
 LANGUAGE: English

Novel liposome useful for activating dendritic cells or as  
 immunomodulating carriers for antigens in vaccines, comprises a  
 chloroform soluble and extractable total polar  
 lipid of *Mycobacterium* species - *Mycobacterium*  
*bovis* or BCG lipid, chloroform soluble  
 liposome characterization useful for cancer and infection therapy  
 ABSTRACT: DEFWENT ABSTRACT: NOVELTY - A liposome (I) comprising a  
 chloroform soluble and extractable total polar  
 lipid of *Mycobacterium* spp., is new. DETAILED DESCRIPTION -  
 INDEPENDENT CLAIMS are also included for the following: (1) a  
 liposome (II) comprising an isolated lipid fraction  
 in biologically pure form from total polar lipids of *M.*  
*bovis* *Bacillus Calmette-Guerin* (BCG) and an associated  
 antigen; (2) a liposome vaccine composition (III) comprising (I)  
 or (II), where the liposome contains an associated antigen; and  
 (3) preparation (M) of (I) or (II) by drying chloroform  
 soluble and extractable lipid and then hydrating the  
 dried lipid at a temperature of 65-75degreesC in water or  
 phosphate buffered saline (PBS). BIOTECHNOLOGY - Preferred  
 liposome (I) comprises a chloroform soluble and  
 extractable polar lipid of *M bovis* BCG  
 which is in biologically pure form. The chloroform soluble  
 and extractable polar lipid comprises at least one  
 of phosphatidylinositol (PI), phosphatidylinositol mannoside  
 (PIM), phosphatidylinositol di-mannoside (PIM2), mono  
 and dimethylated forms of PIM and PIM2 (such as palmitoyl-PIM or  
 palmitoyl-PIM2), acylated-phospholipids of 899, 1139 and 1155  
 m/z, phosphatidylethanolamine and cardiolipid. The chloroform  
 soluble and extractable lipid is an  
 acyl-phosphoglycerophosphate lipid of m/z 899, 1139 or 1155  
 comprising two sn-1,2 fatty acyl chains...

... first chain is tuberculosteric acid and a second chain is palmitic acid  
 (C16:0). The chloroform soluble and extractable  
 polar lipid is obtainable by a hot 50% ethanol  
 extraction. In (I) or (II), the lipid ingredient is  
 synthesized chemically to correspond to the structure of a lipid  
 isolated in biologically pure form from a *Mycobacterium* (I)  
 additionally comprises lipid phosphatidylethanolamine in  
 biologically pure form (I) comprises the chloroform  
 soluble and extractable polar lipid of *M.*  
*bovis* BCG and other lipid selected from  
 phosphatidylcholine, phosphatidylglycerol, cholesterol and its mixture.  
 The liposome is multilamellar or unilamellar. Preferred  
 Composition: In (II) the antigen is a protein. Preferred Method: In  
 (M), the temperature is 65degreesC. The liposome resulting from  
 the method is multilamellar. (M) additionally comprises reducing the

10563731a.txt

size of a multilamellar liposome at a temperature of 65degreesC to yield a unilamellar liposome. An antigen is entrapped in the multilamellar or unilamellar liposome by inclusion of the antigen in water or PBS. ACTIVITY - Cytostatic; Immunomodulator. MECHANISM OF ACTION...

...in all 5 mice in a naive group within 12 days. Injection of antigen-free BCG liposomes resulted in a modest decline in tumor growth, where only 2 mice out of 5...

...of tumor growth was seen. Considerably more protection was seen for mice immunized with the BCG ovalbumin (OVA) liposome vaccine, where all mice tumors were less than 250 mm<sup>2</sup> after 12 days and remained...

...life and is stable to the conditions found upon vaccination of an animal. EXAMPLE - Total lipid extracts were obtained from frozen-thawed cell pastes of Bacillus firmus or from fresh cell paste of Mycobacterium bovis by adding a one-phase solution of methanol, chloroform and water (2:1:0.8, v/v) in a ratio of 15 g cell dry weight/l. After 16 h the cellular debris was collected by centrifugation and re-extracted twice more. Extracts were pooled and made biphasic by addition of chloroform and water by the Bligh and Dyer method. Polar lipids in the chloroform bottom phase were freed of neutral lipids by differential solubility in cold acetone. Polar lipids, insoluble in acetone, were dried and dissolved into chloroform as the chloroform extractable total polar lipids. Bacillus Calmette-Guerin (BCG) total lipids dissolved in chloroform were filtered using a 0.45 micron nylon syringe filter, to ensure there was no carry over of whole cells into the lipid extract. Preparation of B. subtilis BCG liposomes was as follows: About 30 mg of total polar lipids in chloroform were dried under a nitrogen stream followed by 1 hour under vacuum. Hydration was routinely...

...for 2-3 hour at 65degreesC with shaking. To investigate the effect of temperature on liposome formation, hydration was allowed to occur at 35-75degreesC in 10degreesC steps. Average vesicle diameters...

...Preparations were then freeze-dried and re-hydrated in phosphate buffered saline (PBS) at 65degreesC. Liposomes were left overnight at 4degreesC to anneal, then any OVA not associated with the liposomes was removed by ultracentrifugation and washing liposomes with PBS thrice. The final liposome pellets were re-suspended into PBS, and liposomes were filter-sterilized using 0.45 micron filters. Entrapped OVA was quantified after lipid removal and dry weights determined, as above. Average diameters were measured in a 5 mW He/Ne laser particle size. BCG liposomes were made from the isolated lipid fractions obtained by the above method. (46 pages)

DESCRIPTIONS: Mycobacterium bovis, BCG lipid, chloroform soluble liposome, dendrite cell activation, immunomodulator, appl. cancer, infection therapy, vaccine bacterium lipofection transfection cytostatic (22, 19)

13/3, K/13 (Item 2 from file: 357)  
DIALOG(R) File 357: Derwent Biotech Res.  
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0060519 DBR Accession No.: 87-04867 PATENT  
Lipopolysaccharide and its production - using Mycobacterium  
Page 59

tuberculosis etc.; antitumor

PATENT ASSIGNEE: Gelia-Shinyaku 1987

PATENT NUMBER: JP 62004701 (Kokai) PATENT DATE: 870110

WIPO ACCESSION NO.: 87-046805 (8707)

PRIORITY APPLIC. NO.: JP 85141566 APPLIC. DATE: 850629

NATIONAL APPLIC. NO.: JP 85141566 APPLIC. DATE: 850629

LANGUAGE: Japanese

Lipopolysaccharide and its production - using *Mycobacterium tuberculosis* etc.; antitumor

ABSTRACT: A lipopolysaccharide comprising 80-95% polysaccharide comprising D-arabinose and D-mannose, and 5-20% of a fatty acid is described which has cytostatic, immunoregulatory, cell-activating...

...production is simple and gives a high yield. A suitable microorganism is used; e.g. *Mycobacterium tuberculosis*, *Mycobacterium bovis* or *Propionibacterium acnes*. In an example, *M. tuberculosis* strain Aoyama B was cultured for 5 wk, and the dead cells were treated in a French press. The supernatant obtained was extracted with ethanol and centrifuged, and the precipitate was washed with ethanol and ethyl ether. The precipitate was treated with amylase and glucosylase (EC 3.2.1.3) to give crude lipopolysaccharide which was dissolved in pyridine and extracted with methanol and chloroform-methanol. The precipitate was redissolved and subjected to Sepharose 4B chromatography, and the solution was subjected to dialysis and lyophilization to give the lipopolysaccharide. (5pp)

DESCRIPTION: lipopolysaccharide prep., purification, *Mycobacterium tuberculosis*, *Mycobacterium bovis*, *Propionibacterium acnes* etc. culture, antitumor, antibiotic, immunostimulant act. etc. bacterium

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T cell activation by lipopeptide antigens. (Reports)

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T cell activation by lipopeptide antigens. (Reports)

AUTHOR ABSTRACT: Unlike major histocompatibility proteins, which bind peptides, CD1 proteins display lipid antigens to T cells. Here, we report that CD1a presents a family of previously unknown lipopeptides from *Mycobacterium tuberculosis*, named dihydrooxymycobactins because of their structural relation to mycobactin siderophores. T cell activation was mediated by the (alpha)(beta) T cell receptors and was...

...components of these antigens. These studies identify a means of intracellular pathogen detection and identify lipopeptides as a

biochemical class of antigens for T cells, which, like conventional peptides, have a...

TEXT:

...molecular mechanism of antigen presentation by CD1 involves insertion of the alkyl chains of amphipathic lipids into a deep hydrophobic groove formed by the (alpha)1 and (alpha)2 domains of...

...they can directly contact T cell receptors (TCR) (7-9). CD1a-restricted T cells recognize mycobacteria-infected cells and have antibacterial effects, suggesting a possible role in host defense (5, 10...  
...candidate antigens presented by CD1a, TCR (alpha) and (beta) chains from the CD1a-restricted and mycobacteria-specific T cell line CD8-2 were cloned and transfected into J.RT3-T3.5...

...M. tuberculosis cell walls. Antigenic factors capable of J.RT3-CD8-2 activation were efficiently extracted from whole mycobacteria by using chloroform:methanol (2:1), suggesting that the antigens were lipids, which were not covalently bound to the arabinogalactan complex of the mycobacterial cell wall (12). Elution of the stimulatory lipids from silica columns in polar solvents, such as methanol, indicated that the antigens displayed characteristics of polar lipids. Purification by high-performance liquid chromatography (HPLC) led to the isolation of a fraction that contained a set of structurally related compounds, which, by mass spectrometry analysis, yielded a...

...CD8-2 (Fig. 1A). T cell activation was not seen with other known CD1-presented lipid antigens such as mycolic acid, glucose monomycolate, or mannosyl phosphosiprenoids (Fig. 1B). Also, 838 did not activate polyclonal T cells or J.RT3 transfectants expressing TCRs that are specific for lipid antigens presented by CD1b or CD1c (Fig. 1B) (13-15). Together, these studies indicated that...  
...197, which were each 16 u (the mass of oxygen) smaller than the previously described mycobactinic acid and cobactin fragments of mycobactin, a known mycobacterial lipopeptide with iron-scavenging properties (16, 17). Therefore, we named the antigen dihydrooxymycobactin (DDM 838). Identification...

...MS/MS products at  $m/z$  727 and 84 indicated that the hydroxyllysines found in mycobactin were substituted by lysines in the proposed structure for DDM (17). The presence of lysine...

...amino acid, (alpha)-methyl serine, instead of serine and threonine, which are present in most mycobacterial mycobactins (12, 16, 18). The identity of (alpha)-methyl serine as a component of DDM was...

...cyclized lysine (Fig. 2B).  
(FIGURE 2 OMITTED)

Dihydrooxymycobactin most likely functions as an intermediate in mycobactin synthesis. The mycobactin locus in *M. tuberculosis* encodes mycobactin synthase genes, MbtA to MbtJ, which function as a nonribosomal peptide synthesis pathway (20). Previously proposed schemes of mycobactin biosynthesis have emphasized a likely role of MbtA, MbtB, MbtC, MbtD, MbtE, and MbtF in...

...salicyl moiety and synthesizing the peptide (Fig. 2D) (19, 21, 22). The final steps in mycobactin synthesis were thought to involve peptide termination by intramolecular attack of the lysine side chain...

...by suggesting that the lysines are incorporated into the peptide and subsequently hydroxylated to yield mycobactins (Fig. 2D). The two hydroxyl moieties, which are present in mycobactin but absent in DDM, form two sites, which mediate high-affinity ( $\sim 10^{-8}$  sup. -26) M...

... Consistent with the predicted roles of these hydroxyl groups in iron binding, we found that mycobactin was detected in the iron-bound form solely as ((M + Fe-2H).sup.+ ) at m...

...affinity at or near the bacteria-host interface and deliver iron to the bacterium (23). Mycobacteria produce mycobactin and related siderophores, whose synthesis is triggered by derepression of mycobactin synthase genes during growth in low-iron conditions (24). This process normally occurs during growth...

...human macrophages (25). These considerations suggested that DDM might be synthesized as an intermediate in mycobactin production during intracellular infection. We found that DDM-specific T cell activation occurs efficiently in...

...produce DDM at all (Fig. 3A). Because CD1a-restricted T cells are able to kill mycobacteria-infected cells (26), CD1a presentation of DDM may represent an early warning system for intracellular...

...of DDM structure in mediating T cell activation, we used HPLC to isolate several natural lipopeptides from *M. tuberculosis*. In addition to DDM-838 (Fig. 3B, peak E), *M. tuberculosis* produced...

...cis conformation (Fig. 2C). Whereas DDM-838 gave the most potent T cell response, homologous lipopeptides that had shorter or saturated fatty acids were substantially less stimulatory (Fig. 3C). Natural mycobactins were not recognized, suggesting that the hydroxylation of the lysine residues prevents T cell recognition (Fig. 3C). Also, lipid fractions containing mycobactin acid, which corresponds to a truncated lipopeptide lacking the butyric acid lysine moiety (Fig. 2B, m/z 642 fragment), were recognized weakly or...

...peptide and the length and saturation state of the fatty acyl chain.

These studies identify lipopeptides as a biochemical class of antigens for T cells, which share structural features of MHC...

...the predicted TCR contact surface (8). The A' pocket is largely hydrophobic, with no obvious polar groups that could hydrogen bond with the peptidic portion of DDM in the way that...

...Fig. 3D). Although the orientation of the peptidic moiety cannot be predicted precisely, the only polar residues in the binding groove are located at the A'-F' junction, so it seems...

...encoded peptide sequences, which are post-translationally modified by acylation so that their structures resemble mycobacterial DDM but are highly varied in their peptide sequences (29). The autoreactivity of T cells...

...31). These observations raise the possibility that CD1 might also function to present structurally diverse lipopeptides encoded in the DNA of bacteria, viruses, or mammalian cells.

#### References and Notes

(1.) 1...

...Protein Struct. Funct. Genet. 11, 281 (1991).

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